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VOLUME 37 AUGUST 1959 NUMBER 8

HYDROGENOLYSIS OF CARBOHYDRATES

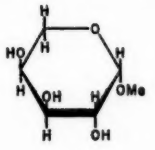
VII. METHYL β-L-ARABOPYRANOSIDE-1-C^{14} [1]

THOMAS FRANCIS[2] AND A. S. PERLIN

ABSTRACT

Methyl β-L-arabopyranoside-1-C^{14} was hydrogenolyzed in the presence of copper chrome oxide catalyst at 250° C, yielding an approximately equimolar mixture of optically inactive *cis*- and *trans*-3,4-dihydroxytetrahydropyran-C^{14}, together with 2,3-dihydroxypentane-C^{14}. The latter was formed by reductive ring-opening of the tetrahydropyrandiols. Ether cleavage of each of the cyclic diols afforded 1,2,3,5-tetrahydroxypentane-C^{14} in which the tracer was distributed about equally between carbons 1 and 5. Carbon-14 in the pentanediol was distributed in a similar manner. The results show that both the 2- and 4-hydroxyl groups of the original pentoside are prone to reductive cleavage, and that *cis*- and *trans*-glycol groups in the cyclic diols are formed by isomerization. They suggest that hydrogenolysis of the methoxyl group takes place initially, accompanied by isomerization, to give a mixture of tetrahydropyrantriols in which the 2- and 4-hydroxyl groups have equivalent reactivity.

In Part V of this series (1) methyl β-L-arabopyranoside (I) was shown to isomerize readily at 180° C in the presence of hydrogen and copper chromium oxide catalyst to a mixture of methyl D- and L-pentosides. This finding offered an explanation of the earlier report (2) that the arabinoside is hydrogenolyzed at 250° to form optically inactive *cis*- and *trans*-3,4-dihydroxytetrahydropyran (dihydro-DL-arabinal and -DL-xylal), rather than the expected L-isomers (II and III, respectively). Clearly, the glycosidic methoxyl group is easily hydrogenolyzed and the 3-hydroxyl group, though isomerized (1), is stable, but it was not possible to decide from these data whether the 2- or 4-hydroxyl group (or both) is cleaved reductively. In the present study this problem has been examined by tracer techniques using methyl β-L-arabopyranoside-1-C^{14}.



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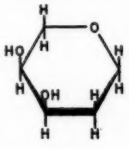

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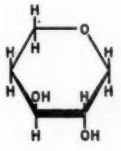

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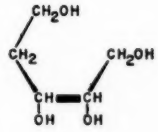

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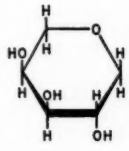

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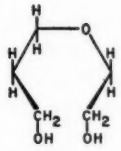

VI

[1]*Manuscript received April 13, 1959.*
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[2]*National Research Council of Canada Postdoctorate Fellow, 1957–58.*

The dihydroglycal-C^{14} fraction, isolated as the major product from hydrogenolysis of the labelled L-arabinoside at 250°, comprised an approximately equimolar mixture of *cis*- and *trans*-isomers, in agreement with the earlier finding (2). Acetonation of the mixture afforded the *O*-isopropylidene derivative of the *cis*-diol, and the *trans*-isomer remaining was freed from a small proportion of unacetonated *cis*-diol by selective lead tetraacetate oxidation of the latter. The purified isomers were optically inactive.

Acetolysis of the diols-C^{14} in the presence of boron trifluoride (3) yielded from each the tetraacetate of 1,2,3,5-tetrahydroxypentane (IV). Following deacetylation the tetritols were oxidized with periodate, and the formaldehyde produced was isolated as the dimedon derivative or the 2,4-dinitrophenylhydrazone. Since the formaldehyde was derived either from carbon 1 or carbon 5 of the original methyl L-arabinoside, or from both, its specific activity provided a measure of the percentage survival of the 2- and 4-hydroxyl groups of the glycoside. Thus, if only the 4-hydroxyl group had been hydrogenolyzed all of the carbon-14 should have been located in the formaldehyde, but inactive formaldehyde should have been obtained if the 2-position was attacked exclusively. In fact, the formaldehyde from the *cis*- and *trans*-isomers contained 40–45% of the total activity (Table I), showing clearly that the 2- and 4-hydroxyl groups were cleaved

TABLE I

Specific activity of products from methyl β-L-arabopyranoside-1-C^{14}

Compound	Specific activity (mμc/mmole)	Per cent reduction at C_2	Per cent reduction at C_4
Methyl β-L-arabopyranoside-1-C^{14}	47.2		
cis,trans-3,4-Dihydroxytetrahydropyran-C^{14}	47.4		
Formaldehyde from *cis*-3,4-dihydroxytetrahydropyran-C^{14} *			
As dimedon (sp. activity 1.25 mμc/mM CO_2)	21.2		44.8
As 2,4-dinitrophenylhydrazone (sp. activity 2.73 mμc/mM CO_2)	19.1	58.1†	39.0
Formaldehyde from *trans*-3,4-dihydroxytetrahydropyran-C^{14}*			
As dimedon (sp. activity 1.25 mμc/mM CO_2)	21.2		45.1
As 2,4-dinitrophenylhydrazone (sp. activity 2.63 mμc/mM CO_2)	18.4	57.2†	40.5
Acetaldehyde from 2,3-dihydroxypentane-C^{14}			
As 2,4-dinitrophenylhydrazone (sp. activity) 2.10 mμc/mM CO_2)	16.8		35.5
Propionaldehyde from 2,3-dihydroxypentane-C^{14}			
As 2,4-dinitrophenylhydrazone (sp. activity) 3.07 mμc/mM CO_2)	27.6	58.5	

*By periodate oxidation of derived 1,2,3,5-tetrahydroxypentane.
†Calculated by difference from average of the C_4 values.

reductively almost to the same extent. The results show also, contrary to the original interpretation (2), that the presence of *cis*- and *trans*-1,2-diol groups in the products is not related necessarily to the occurrence of such groups in the methyl L-arabinoside, but to isomerization. Thus, *cis*- and *trans*-glycol groups are located in the tetrahydropyrandiols at positions corresponding to both the 2,3- and 3,4-positions of the glycoside.

The approximately equivalent reactivity of the 2- and 4-hydroxyl groups in methyl L-arabinoside contrasts with hydrogenolysis mainly of the 4-position in methyl α-D-glucopyranoside (4, 5). Possibly hydrogenolysis of the pentoside is initiated at carbon 1 giving rise, also as a result of isomerization (1), to a mixture of 1,5-anhydropentitols (e.g., V). In the latter mixture the 2- and 4-hydroxyl groups would be more nearly equivalent than in the parent glycosides and hence reduced at about the same rate. The survival in each molecule of one of these groups together with the 3-hydroxyl group may be attributed to the resistance of 1,2-diols and the instability of 1,3-diols to hydro-

genolysis (6). Relatively greater reactivity of the 4-position in methyl D-glucoside possibly is associated with the influence of the primary carbinol group.

About one-third of the hydrogenolysis product consisted of a low-boiling oil which yielded a *p*-nitrobenzoate corresponding to that of a pentanediol. This product was found to be mainly 2,3-dihydroxypentane, for it consumed about one mole of periodate with production of acetaldehyde and propionaldehyde. Previously, methoxypentanediols were reported present in the reaction mixture (2), but, since polyols may give spurious methoxyl values (7), it is likely that the product actually encountered was the pentane-2,3-diol. The diol was produced also by hydrogenolysis of the isolated tetrahydropyrandiols, and hence was a secondary reaction product resulting from reductive cleavage of the cyclic ether group. When the C^{14}-labelled glycoside was used as starting material the propionaldehyde obtained from the pentanediol by periodate cleavage accounted for 58%, and the acetaldehyde 36%, of the tracer (Table I). These data show again that the 2- and 4-positions of the methyl pentoside are both subject to reduction, and correspond closely to the data obtained with the tetrahydropyrandiols.*

Another possible procedure was examined for evaluating the distribution of tracer in the tetrahydropyrandiols. The diols were oxidized with periodate and the resulting dialdehydes reduced to give the corresponding dihydroxy ether (VI). Cleavage of VI was expected to afford ethylene glycol and 1,3-dihydroxypropane, the specific activities of which would indicate the relative proportion of carbon 1 from the L-arabinoside-C^{14} in each fragment. However, the ether linkage of VI proved to be particularly resistant, and the low yield of products obtained made the procedure unattractive for use with the small quantity of radioactive diols available.

EXPERIMENTAL

Methyl β-L-arabopyranoside-1-C^{14}, m.p. 171–173°, was prepared by methanolysis (8) of L-arabinose-1-C^{14}.

Paper chromatography was carried out with Whatman No. 1 paper using *n*-butanol: ethanol:water (40:11:19) as solvent and ammoniacal silver nitrate as the spray reagent (9).

Melting points are corrected.

Radioactive samples were combusted and the specific activity of the carbon dioxide liberated was measured by the procedure of Buchanan and Nakao (10). Reproducibility of the measurements was about ±3%.

Hydrogenolysis of Methyl β-L-Arabopyranoside-1-C^{14}

Methyl β-L-arabopyranoside-1-C^{14} (47.6 mμc/mmole) (6.0 g) in dioxan (100 ml) was shaken for 5 hours at 250° with copper chromium oxide catalyst (1.25 g) in an atmosphere of hydrogen at 2000 p.s.i. The syrupy product (3.2 g) obtained after removing the catalyst and evaporating the solvent was found by paper chromatography to consist of two main components (R_F 0.52 and 0.82). Distillation at 0.3 mm afforded the faster-travelling of these components as an oil (1.0 g), b.p. 51–65° (bath temp.), n_D^{20} 1.4404, and the second as an oil (1.5 g), b.p. 81–90°, n_D 1.4630. The latter product was identified by paper chromatography as 3,4-dihydroxytetrahydropyran and, by plotting its rate of uptake of lead tetraacetate, was found to consist of a 45:55 mixture of *cis*- and *trans*-isomers (cf.

**Cleavage of the ether ring in tetrahydropyran derivatives with boron trifluoride – acetic anhydride has been found in at least one instance to produce positional isomers (3). Formation of* IV *from* II *or* III, *however, did not appear to involve such a side reaction (3). The distribution of tracer in 2,3-dihydroxypentane affords an independent check on the latter acetolysis reaction, by showing that labelling in the tetrahydroxypentane is that expected for normal ring-opening of the cyclic ether.*

ref. 2). Separation of the isomers on chromatograms could not be effected by adding boric acid to the solvent, nor by column chromatography on cellulose using benzene: ethanol:water (500:50:1).

cis-3,4-Dihydroxytetrahydropyran-C^{14}

The higher-boiling oil (1.0 g) was dissolved in acetone (50 ml) containing 1% concentrated sulphuric acid. After 24 hours at room temperature the solution was neutralized with anhydrous potassium carbonate, filtered, and evaporated. The residual syrup was dissolved in water and the solution extracted 3 times with ether. Acetic acid (10 ml, 30%) was added to the extract, the ether evaporated, and the solution heated on the steam bath for 1 hour. Removal of the solvent gave a syrup (R_F 0.51) which was purified by distillation. Weight 0.27 g, $[\alpha]_D^{24}$ 0°±0.1° (*c*, 2, satd. borax). Treatment of the product with *p*-toluenesulphonyl chloride in pyridine gave *cis*-di-*O*-*p*-toluenesulphonyl-3,4-dihydroxytetrahydropyran, m.p. 131–132°; the infrared absorption spectrum was indistinguishable from that of an authentic specimen.

trans-3,4-Dihydroxytetrahydropyran-C^{14}

The water-soluble fraction from the acetonation procedure (0.56 g) appeared, from its rate of lead tetraacetate uptake, to contain about 15% of *cis*-isomer. The latter was preferentially removed by lead tetraacetate oxidation and the product worked up as described earlier (2), affording an oil (0.31 g), R_F 0.57, $[\alpha]_D^{24}$ 0°±0.1° (*c*, 2, satd. borax). The derived tosyl ester had m.p. 159–162°, and gave an infrared absorption spectrum indistinguishable from that of *trans*-di-*O*-*p*-toluenesulphonyl-3,4-dihydroxytetrahydropyran.

1,2,3,5-Tetrahydroxypentane-C^{14}

The tetritol was prepared from the *cis*- and *trans*-diols by acetolysis in the presence of boron trifluoride as described earlier (3), and separated from a small proportion of starting material by column chromatography on cellulose using *n*-butanol. The *trans*-isomer (0.31 g) and the *cis*-isomer (0.27 g) each yielded 0.19 g of tetritol.

Periodate Oxidation of 1,2,3,5-Tetrahydroxypentane-C^{14} *and Isolation of Formaldehyde*

(*a*) Oxidation of the tetritol with periodate and recovery of liberated formaldehyde as the dimedon derivative was carried out according to the procedure of Bell (11). In a typical experiment, the tetritol (0.10 g) derived from *cis*-3,4-dihydroxypyran-C^{14} yielded 0.20 g of formaldehyde dimedon, m.p. and mixed m.p. 192–193°.

(*b*) In a typical experiment, the tetritol (0.09 g) in water (20 ml) was oxidized with periodic acid (0.40 g) for 4 hours. Dowex-1 resin (bicarbonate form) was added until a negative starch–iodide test was obtained, the solution was concentrated, the distillate being trapped in a solution of 2,4-dinitrophenylhydrazine in dilute hydrochloric acid. After it was dried, the recovered hydrazone was purified by chromatography on silicic acid:Supercel (2:1) using Skelly B containing 5% ether (12). Weight 0.09 g, m.p. 166–167°, undepressed by admixture with formaldehyde 2,4-dinitrophenylhydrazone.

2,3-Dihydroxypentane-C^{14}

The low-boiling oil consumed 0.96 mole of periodic acid per mole, producing 0.86 mole of acetaldehyde (estimated colorimetrically (13)), and 0.13 mole of formaldehyde (estimated colorimetrically (14)). On treatment with excess *p*-nitrobenzoyl chloride in hot pyridine it afforded a di-*O*-*p*-nitrobenzoate, m.p. 168–169° after recrystallization

from ethyl acetate. Calc. for $C_{19}H_{18}O_8N_2$: C, 56.71%; H, 4.51%; N, 6.96%. Found: C, 56.80%; H, 4.50%; N, 6.73%.

The oil (0.10 g) in water (25 ml) was treated with periodic acid (0.20 g) for 1.5 hours, the solution was neutralized with Dowex-1 resin, and a solution of 2,4-dinitrophenylhydrazine in dilute hydrochloric acid was added. A precipitate which formed was collected, dried, and chromatographed on silicic acid:Supercel as described above. Two fractions were isolated, the first having m.p. 157°, after recrystallization from ethanol, undepressed by admixture with propionaldehyde 2,4-dinitrophenylhydrazone. Calc. for $C_9H_{10}O_4N_4$: C, 45.38%; H, 4.23%. Found: C, 45.85%; H, 4.01%. The second fraction, recrystallized from ethanol, had m.p. 159–164°. Calc. for $C_8H_8O_4N_4$: C, 42.90%; H, 3.60%. Found: C, 43.30%; H, 3.72%.

2,3-Dihydroxypentane from Hydrogenolysis of 3,4-Dihydroxytetrahydropyran

A mixture of *cis*- and *trans*-3,4-dihydroxytetrahydropyran (4.4 g) was treated for 24 hours under the hydrogenolysis conditions described above. The product (1.5 g), which on chromatographic examination appeared to consist mainly of 2,3-dihydroxypentane, distilled at 45–55°/0.05 mm (bath temp.) to give an oil, having an infrared absorption spectrum indistinguishable from that of 2,3-dihydroxypentane, n_D^{25} 1.4412. The derived *p*-nitrobenzoate had m.p. 165–167°, undepressed by admixture with 2,3-dihydroxypentane di-*p*-nitrobenzoate; the X-ray diffraction patterns of the two diesters were indistinguishable.

Hydroxyethyl-(3-hydroxy)n-propyl Ether (VI)

A mixture of *cis*- and *trans*-3,4-dihydroxytetrahydropyran (2.4 g) in water (40 ml) was treated with periodic acid (4.8 g) for 5 hours. Excess periodate and iodate were removed with Dowex-1 resin (bicarbonate form), the solution was evaporated to half volume and added dropwise to a solution (30 ml) of sodium borohydride (1.5 g). After 18 hours excess Amberlite IR-120 was added, the filtrate was concentrated to dryness, and boric acid removed by repeated (4 times) addition and evaporation of methanol. The product (1.65 g), b.p. 115–125°/0.8 mm (bath temp.), was a viscous oil, n_D^{24} 1.4515, R_F 0.66. It yielded a *p*-nitrobenzoate which solidified when taken up in ether and, after four recrystallizations from methyl ethyl ketone – ether, had m.p. 98–100°. Calc. for $C_{19}H_{18}O_9N_2$: C, 54.55%; H, 4.34%; N, 6.70%. Found: C, 54.73%; H, 4.26%; N, 6.54%.

Cleavage of the Dihydroxy Ether (VI)

(*a*) Treatment of the dihydroxy ether with acetic anhydride – boron trifluoride as described above for 3,4-dihydroxytetrahydropyran yielded only trace amounts of cleavage products.

(*b*) The syrupy ether (0.15 g), in acetic anhydride (2 ml) containing freshly fused zinc chloride (0.15 g), was heated on the steam bath for 12 hours. Cold saturated potassium carbonate was added and the neutral solution extracted three times with chloroform. Evaporation of the chloroform solution yielded a residue which was treated with 0.1 *M* sodium methoxide for 18 hours. The solution was neutralized with Amberlite IR-120 and concentrated, giving a dark syrup (0.074 g). Chromatographic examination indicated that the product consisted of ethylene glycol and 1,3-dihydroxypropane, and a minor, slower-moving component which was not starting material. The spot corresponding to ethylene glycol was absent from the chromatogram when the mixture was treated beforehand with periodic acid, and formaldehyde was produced in the oxidation as shown by isolation of formaldehyde dimedon (6 mg from 30 mg of cleavage product), m.p. and mixed m.p. 186–189°.

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The authors express their gratitude to Dr. A. C. Neish for a generous sample of L-arabinose-1-C^{14}. Dr. P. A. J. Gorin contributed valuable suggestions. Carbon-14 assays were carried out by J. Dyck, and microanalyses by T. Mazurek; infrared spectra and X-ray diffraction patterns were prepared by Inez Gaffney and M. Granat.

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ADSORPTION OF STERICALLY HINDERED PHENOLS ON CARBON[1]

OWEN H. WHEELER[2] AND ERIC M. LEVY

ABSTRACT

The Freundlich isotherms for the adsorption of some ortho-alkylated phenols on carbon from cyclohexane solution have been determined. The minimum surface area covered by the adsorbed phenols is compared with the area of the molecules themselves. Large alkyl groups ortho to the hydroxyl group greatly reduce the adsorption.

INTRODUCTION

The importance of steric effects in reactions occurring in a homogeneous phase is now well understood (1), but few data are available concerning the effect of steric hindrance in heterogeneous reactions. The kinetic rate-controlling step in such reactions is often the adsorption of the reactants on the surface of an adsorbent, and such a process will be considerably influenced by steric effects.

The adsorption of a series of ortho-alkylated phenols on carbon from cyclohexane solution has been studied. Phenols were chosen since they should be strongly adsorbed and can be easily analyzed. Carbon is a suitable adsorbent since it contains neither strongly acidic nor basic groups, and cyclohexane is a convenient inert solvent which is available in a state of high purity.

The effective surface area of the carbon used was first determined by the standard method (2) of adsorption of nitrogen at liquid air temperature.

The results of the adsorption of the phenols were expressed in the form of the Freundlich isotherm equation ($x/m = k.c^n$, where x is the amount adsorbed by m grams of adsorbent, and c is the equilibrium concentration of the adsorbate) as plots of x/m against c (Fig. 1). In all cases the graphs show limiting values of the amounts of phenol adsorbed, which must correspond to the formation of unimolecular layers.

EXPERIMENTAL

Reagents

Carbon

This was a sample of Darco G-60 adsorbent carbon supplied by the Atlas Powder Company of Canada, Ltd. The manufacturer's analysis was: ash content 2–5%, water solubles 0.1–0.2%, acid solubles 0.5%, pH of water extract 5–6, moisture 5–10%. The loss of weight of a sample dried to constant weight at 145° C corresponded to a moisture content of 5.2%. The sample used was dried under these conditions and stored over phosphorus pentoxide.

Gases

Nitrogen and helium were Canadian Liquid Air Company's pure samples and were dried prior to use.

Phenols

Phenol (Allied Chemical and Dye Corporation, absolute), *p-tert*-butylphenol (Dow Chemical Company), and 2,6-dimethylphenol (Aldrich Chemical Company) were used without further purification. 2,6-Diisopropylphenol (Aldrich) was vacuum-distilled twice.

[1]*Manuscript received February 19, 1959.*
Contribution from Department of Chemistry, Dalhousie University, Halifax, N.S.
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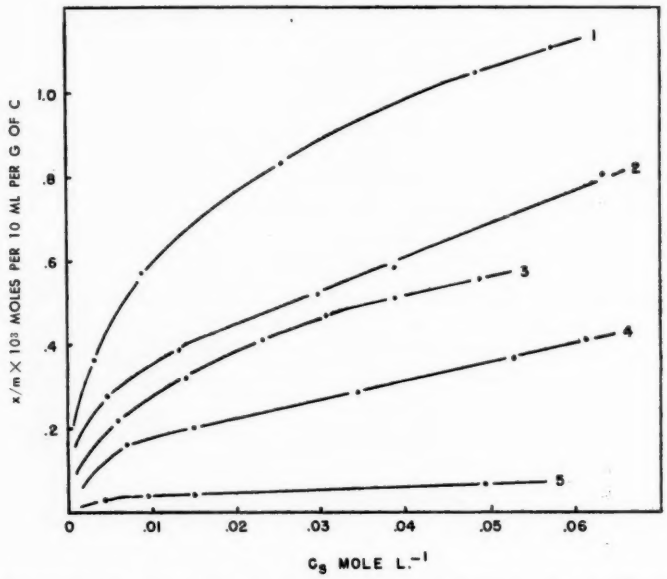

FIG. 1. Adsorption of phenols. 1. Phenol. 2. 2,6-Dimethylphenol. 3. *p-tert*-Butylphenol. 4. 2,6-Diisopropylphenol. 5. 2,6-Di-*tert*-butylphenol.

A yellow-colored impurity persisted in the product. 2,6-Di-*tert*-butylphenol (Aldrich) was recrystallized twice from ethanol.

The physical constants of the phenols are given in Table I.

TABLE I

Physical constants of phenols

	M.p./b.p.[a]	λ_{max}[b]
Phenol	43.0° (41°)	271 (1520), 276 (1450)[c]
p-tert-Butylphenol	97° (100°)	277 (1810)
2,6-Dimethylphenol	49.0° (49.0°)	273 (1450), 276 (1400)[c]
2,6-Diisopropylphenol	107.5°/110 mm, n_D^{20} 1.5124	273 (1700), 276 (1650)[c]
2,6-Di-*tert*-butylphenol	37.0° (39°)	272 (1410), 275 (1340)[c]

[a]Literature values in parentheses, ref. 16. [b]Wavelength of maximal absorption in mμ. Molar extinction coefficients (ε) in parentheses. [c]Inflection.

Aromatic Hydrocarbons

Benzene, *o*- and *p*-xylene, isopropyl- and *tert*-butyl-benzene, and mesitylene were Eastman-Kodak white label grade and were distilled before use (see Table II for physical constants).

Solvents

Cyclohexane was Fisher or Eastman-Kodak spectro-grade and was used as received. The 95% alcohol was a commercial grade which was free from aromatics as judged from its ultraviolet adsorption.

TABLE II

Physical constants of hydrocarbons

	B.p.[a]	n_D^{25}	λ_{max}[b]
Benzene	80.2° (80.1°)	1.5000	254.5 (186)
o-Xylene	143.5° (144.9°)	1.5030	263 (245)
p-Xylene	138.5° (138.3°)	1.4924	268.5 (243) 274.5 (269)
Isopropylbenzene	152.5° (152.4°)	1.4875	260 (180)
tert-Butylbenzene	170.0° (169.1°)	1.4894	278 (178)
Mesitylene	165.0° (164.7°)	1.4922	255 (193)

[a]Literature values in parentheses. [b]Wavelength of principal maxima in mμ. Molar extinction coefficients in parentheses.

Specific Surface Area of Carbon

The apparatus used was similar to that of Emmett and Brunauer (2) and consisted of an adsorption bulb connected by narrow bore glass tubing to a calibrated gas burette and a mercury manometer, attached to a conventional high vacuum line. The dead space in the adsorption bulb containing the carbon specimen was determined from pressure–volume measurements using helium. A series of pressure–volume experiments were then carried out with pure nitrogen while the adsorption vessel was immersed in liquid air. An adsorption isotherm of residual pressure against volume of nitrogen adsorbed was constructed and gave a limiting value of nitrogen required to form a unimolecular layer at 78° K of 42.0 cm^3 for 0.5424 g of carbon. Using the value of the effective area of nitrogen molecule at −195.8° C of 16.2 $Å^2$ (3), the corresponding specific surface area of the carbon is 1.15×10^8 $meter^2$ per g. This is in agreement with the findings of other workers (3) and Kipling states that "there has recently been a downward trend in surface area values of Darco G from 2123 $meter^2/g$ to 1295 $meter^2/g$" (3).

Adsorption of Phenols on Carbon

Samples of 10 ml of solutions of varying concentrations (0.01 to 0.1 *M*) of the phenols in cyclohexane were shaken with 0.200 g of carbon in 12-ml centrifuge tubes fitted with ground glass stoppers. The shaking was carried out by tumbling the tubes end-over-end at *ca.* 75 r.p.m. with a constant speed motor for ½ hour. It was found that in the case of phenol itself adsorption on the carbon was very rapid for the first 10 minutes and essentially complete after ½ hour. A very slow increase in adsorption took place with a longer time of contact. The suspensions were centrifuged for 5 minutes, and 5-ml portions of the clear solutions were removed with a pipette, care being taken not to disturb the carbon. All these operations were carried out in a constant-temperature room maintained at 20.5±0.5°. The 5-ml aliquots were diluted with 95% ethanol to give solutions of about 4×10^{-4} *M*, and the concentration of unadsorbed phenol was determined by measuring the intensity of ultraviolet absorption at the wavelength of maximal absorption of the phenol (270 to 275 mμ, see Table I). Graphs of the amount of phenol in moles adsorbed per gram of carbon against unadsorbed phenol are given in Fig. 1.

The adsorption of the aromatic hydrocarbons was determined in like manner and the results are expressed graphically in Fig. 2.

Surface Area Occupied by Phenol Molecules

The experimental area of the surface of the adsorbent occupied by one molecule of phenol was calculated (Table III, column 3) from the limiting amount of phenol adsorbed

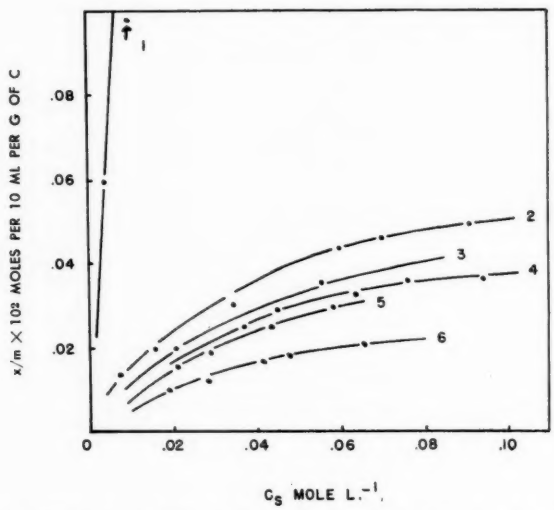

FIG. 2. Adsorption of hydrocarbons. 1. Benzene. 2. Mesitylene. 3. *o*-Xylene. 4. *p*-Xylene. 5. *tert*-Butylbenzene. 6. Isopropylbenzene.

(in moles per 10 ml of solution per gram of carbon) and the known active surface area of the carbon sample.

TABLE III

Surface area occupied by phenol molecules

Phenol	Moles/g 10 ml $\times 10^3$	Exptl. area (A_E)	Calc. area (A_c)	(A_E/A_c)
Phenol	0.97	200	33	6.0
p-tert-Butyl	.52	368	45	8.2
2,6-Dimethyl	.35	550	49	11.2
2,6-Diisopropyl	.175	1090	64	17.0
2,6-Di-*tert*-butyl	.048	3980	64	62.0

The surface area of each phenol molecule in the plane of the benzene ring was calculated (Table III, column 4) using the value of bond distances and the radius of the hydrogen atom given by Pauling (4) and the ring carbon–methyl and carbon–hydroxyl distances of Badger (5). The ratio of the experimental surface area covered by a phenol molecule to the plane surface area of the molecule (assuming "square packing") is given in the last column of Table III.

DISCUSSION

If it is assumed that the phenols are adsorbed with the benzene ring parallel to the surface of the adsorbent, then the fraction of the available surface covered in the case of phenol and *p-tert*-butylphenol is only 1/6 and 1/8, respectively. For the ortho dialkyl-substituted phenols the fraction is 1/11, 1/17, and 1/62 for methyl, isopropyl, and *tert*-butyl groups, respectively. The small fraction of the surface covered even in the case of phenol itself suggests that adsorption of the phenols takes place only at certain "active centers" on the adsorbent. The decreasing adsorption of 2,6-dimethyl and 2,6-

diisopropylphenol is consistent with the increasing steric shielding of the hydroxyl group and suggests that this group is largely responsible for the adsorption. The greatly decreased adsorption of 2,6-di-*tert*-butylphenol must be due to the large steric size of the *tert*-butyl groups, and the effect of their steric hindrance is also manifest in the physical properties (6) and chemical reactions (7, 8, 9) of this phenol. Carlton and Bradbury (10) have studied the paper chromatographic behavior of these phenols and they found that while alkyl groups in the meta- and para-positions have little effect on the adsorption, in the case of ortho-alkylated phenols the adsorption decreases with increasing size of the substituent. Under their conditions 2,6-di-*tert*-butylphenol was not adsorbed at all. The decreased adsorption of *o*-toluic acid as compared with benzoic acid on carbon (11), and of *o*-cresol and *o*-anisidine as compared to their *p*-analogues on silicic acid (12), has also been observed.

Recently Hallum and Drushel (13) have advanced infrared and polarographic evidence that the surface of carbon black contains free hydroquinone and quinone groups. These could constitute the "active centers" for adsorption of the phenols by hydrogen bonding, and since the hydroquinone and quinone groups do not cover the entire free surface it is understandable that the phenols can cover only part of the available surface area.

Though the principal adsorption force will be hydrogen bonding a further possibility is interaction between the π-electrons of the phenol rings and those of the "aromatic structure" of the graphite surfaces on the carbon particles. Experiments with aromatic hydrocarbons (see Fig. 2) show that although benzene itself is easily adsorbed the effect of alkyl substituents is to greatly reduce adsorption. This is true whether there is one, or more than one, group in ortho- or para-positions or whether the groups are methyl, isopropyl, or *tert*-butyl. Thus, since phenol and *p-tert*-butylphenol are adsorbed to similar extents, π-electron interaction cannot contribute to the forces of adsorption to any large extent. However, there is a small difference between these two phenols, which suggests that adsorption is with the plane of the benzene ring parallel to the surface of the carbon, since if the molecule were perpendicular to the surface no difference would be observed. (The electronic effect of the *p-tert*-butyl groups (donating electronic charge to the ring) (14) will increase the acid strength of the phenol and increase the strength of hydrogen bonding, producing an effect which would be opposite to that observed.)

The steric effect of the ortho alkyl groups in the phenols will decrease their acid strengths by inhibiting resonance with the benzene ring (14), and this in turn will decrease the strength of hydrogen bonding. Thus it appears that the ortho-alkylated phenols are adsorbed weakly, due both to the direct steric effect of the alkyl groups preventing hydrogen bonding and to their indirect effect of weakening this hydrogen bonding.

Spectra of the Phenols

The ultraviolet absorption spectra of the phenols shows some interesting effects. Thus *p-tert*-butylphenol absorbs at a higher wavelength and with a higher intensity than phenol itself. This is attributable to the inductive effect of the *tert*-butyl group increasing the electron density in the ring. The displacement to higher wavelength also results in submergence of the inflection at *ca.* 275 mμ which is present in all the other phenols measured.

In the case of 2,6-dimethyl-, 2,6-diisopropyl-, and 2,6-di-*tert*-butyl-phenol, though the wavelengths of the maxima do not change, the intensities of absorption increase and then decrease with increasing size of the group. This must be due to the opposing effect of

increasing inductive effect (which will increase the intensity) and increasing steric effect (which will decrease the intensity) (15) on passing from methyl, through isopropyl, to *tert*-butyl.

ACKNOWLEDGMENTS

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THE ISOLATION AND PROPERTIES OF LIGNINS OBTAINED BY THE ACIDOLYSIS OF SPRUCE AND ASPEN WOODS IN DIOXANE–WATER MEDIUM[1]

J. M. PEPPER, P. E. T. BAYLIS,[2] AND E. ADLER

ABSTRACT

A study has been made of the isolation of a lignin fraction from spruce and aspen wood meals using a low temperature (90–95° C) acidolysis involving a dioxane–water (9:1) solvent medium containing the equivalent of 0.2 *N* hydrochloric acid. The effect of extraction time on the yield of precipitated lignin and ether-soluble material, and on the methoxyl content of these products, was investigated. For both species prolonged extraction times led to greater yields of lignin with lower methoxyl content.

Further acidolysis of isolated spruce lignin led to no significant loss of methoxyl indicating the stability of this group to these reaction conditions. With increasing times of acidolysis of the aspen wood, a slow rise in the carbon–methyl/methoxyl ratio was observed for the isolated lignins. This is in agreement with earlier findings for the spruce lignin. The yields of vanillin and syringaldehyde from aspen lignin on alkaline nitrobenzene oxidation were much less than those from wood meal, and the relative yield of syringaldehyde was higher.

It is suggested that this type of lignin may be only mildly modified during extraction and hence suitable for subsequent chemical investigation. The significance of the findings is discussed.

An attempt has been made to isolate the lignin fraction from both spruce and aspen woods, in yields sufficiently high that the product may be considered representative of the lignin in the wood and yet remain in a form suitable for subsequent extensive chemical investigation. It is well established that rearrangements, which occur during the ethanolysis of wood meal, give rise in both the soluble Hibbert monomers (1) and in the ethanol lignin (2) to an increased percentage of carbon–methyl groupings over that of the original, acetoxy-free, wood meal. This suggested the need for a readily available lignin in which these acid-catalyzed rearrangements could be studied more systematically. The importance of the nature of the extracting solvent in typical alcoholysis reactions has been emphasized by Schuerch (2, 4), who stated, "The low reported yields of lignin alcoholysis products are mainly the result of the slight solubility of the products in the solvent rather than solely the result of polymerization reactions". Other workers (5, 6) have also emphasized the importance of using an aqueous organic solvent system for increased lignin solubility. The well-known alcoholysis procedure for the isolation of lignin suffers primarily from the disadvantage of solvent–lignin interaction. Thus the use of methanol or ethanol was excluded since the ready etherification of various lignin alcoholic groups would yield a product whose analysis for either methoxyl or carbon–methyl respectively would be difficult to interpret.

The use of dioxane in a typical solvolysis reaction has been studied (1), but has led to conflicting reports as to its usefulness. However, dioxane–water appeared to offer many advantages as a solvolysis medium: it has been shown to be a good solvent (5); dioxane is not known to react with lignin to any appreciable extent, and such a system, at reflux, would provide a moderately elevated extraction temperature. The presence of small amounts of a mineral acid (usually hydrochloric acid) are necessary in the lignin solvolysis

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reaction. Concentrations of such acid ranging from 0.01 to 3.8% have been reported (1) but no detailed study appears to have been reported on the effect of this variable on yields of isolated lignins. Schuerch (4) reported that in a series of experiments involving the solvolysis of spruce lignin in a chloroform–ethanol system, the decrease in hydrogen chloride concentration from 1.75 to 0.7% substantially lowered the rate of delignification. Konkin and Rogovin (7), in a study of the delignification of wood using ethylene glycol for ½ hour at 180° C, showed that a slight decrease in the amount of lignin dissolved occurred if the hydrogen chloride concentrations were varied from 0.1 to 0.02%. The most commonly used acid concentration is 0.2 *N* (0.7%) and this is used throughout this research.

A. ISOLATION OF LIGNIN FROM SPRUCE WOOD

In a series of preliminary experiments to compare the suitability of various solvent systems, pre-extracted spruce wood meal was suspended in the solvent medium containing 0.2 *N* (by weight) dry hydrogen chloride and refluxed for 4 hours in a nitrogen atmosphere. The solvents chosen were chloroform–methanol (4:1), dioxane–methanol (9:1) as recommended by Schuerch (3), dioxane, and dioxane–water (9:1). The reaction mixture was filtered, and the filtrate, after neutralization with sodium bicarbonate, was concentrated to a small volume. The lignin was precipitated by forcing this concentrate, as a fine stream, under the surface of 1% sodium sulphate solution. The lignin was removed by centrifugation and decantation and the mother liquors were exhaustively extracted with ether. The residual wood meal, the lignin, and the ether-soluble extract* were dried to constant weight and analyzed for methoxyl content. The results are given in Table I.

TABLE I

Preliminary lignin extraction experiments[a]

Solvent	Residual pulp		Lignin		Ether extract		Total methoxyl recovery, %
	Temp., °C	Recovery, %	Methoxyl, %	Weight, g(% K.L.)[b]	Methoxyl, %	Weight, g(% K.L.)[b]	Methoxyl, %
$CHCl_3$–CH_3OH (4:1) H_2O[c]	55	79.9	6.58	1.35 (19.6)	16.5	—	—	—
$CHCl_3$–CH_3OH (4:1)	55	77.6	6.55	1.0 (14.5)	20.9	0.073 (1.06)	25.2	123
Dioxane–CH_3OH (9:1)	80	54.2	3.48	4.3 (64)	21.4	0.88 (12.8)	27.2	134
Dioxane	96	65.5	4.23	3.52 (51)	12.2	1.41 (20.5)	15.0	110
Dioxane–water (9:1)	94	50.5	2.20	5.13 (74.5)	14.4	1.46 (21.2)	10.9	97.5

[a]Pre-extracted spruce wood (25 g); solvent (200 ml); 0.2 *N* HCl; reflux time, 4 hours, under nitrogen.
[b]Expressed as percentage of the Klason lignin.
[c]The wood meal was first refluxed for 4 hours with 0.2 *N* HCl, then filtered and treated as indicated.

The significant alkylation as indicated by the marked increased total methoxyl content in those experiments using methanol supports this well known reaction of lignin. This alkylation reaction has been studied (8) and explained as being due to the etherification of benzyl alcohol groups or the re-etherification of benzyl ether groups. The effect of an acid treatment of the wood meal prior to the chloroform–methanol extraction was limited. There is an indication that some added methylatable hydroxyl groups were liberated but that some condensation occurred to decrease the solubility of the lignin. The advantage of using aqueous dioxane over dioxane alone is indicated by the significantly increased yield and methoxyl content of the isolated lignin. It would appear that,

**It must be pointed out that the small amounts of dioxane introduced during the precipitation process modify the solubility of the extracted substances.*

in the aqueous system, some carbohydrate or other non-methoxyl-containing fragments that appear with the lignin in the pure dioxane extraction have been separated and appear instead in the ether extract giving rise to the relatively lower methoxyl content of this fraction.

Since it had been shown that the dioxane–water (9:1) solvent system was effective for lignin extraction, the effect of the time of reflux was studied. Similar experiments were conducted with the reflux times of 1, 2.5, 4.0, and 8.0 hours. The components of the reaction mixture were obtained and analyzed as before. The results are given in Table II.

TABLE II

Effect of reflux time on isolation of spruce lignin[a]

Time, hours	Residual pulp		Lignin		Ether extract		Total methoxyl recovery, %
	Recovery, %	Methoxyl, %	Weight, g(% K.L.)[b]	Methoxyl, %	Weight, g(% K.L.)[b]	Methoxyl, %	
1.0	73	3.62	2.25 (32.5)	16.1	0.74 (10.8)	15.9	94.3
2.5	62	2.44	3.77 (55)	15.0	1.23 (17.8)	11.7	90.0
4.0	52	1.73	4.95 (72)	14.3	1.66 (24.1)	10.4	91.5
4.0[c]	50.5	2.2	5.13 (74.5)	14.4	1.46 (21.2)	10.9	97.5
8.0	42.5	1.16	6.56 (95)	12.7	1.95 (28.3)	6.74	89.5

[a]Pre-extracted spruce wood (25 g); dioxane–water (9:1) (200 ml); 0.2 *N* HCl; reflux temperature, 90–94° C, under nitrogen.
[b]Expressed as percentage of Klason lignin.
[c]Included from Table I to indicate order of reproducibility.

There is no evident variation in methoxyl recovery with time of reflux, but the average value of 92.5% appears sufficiently significant to suggest a small but rapid acid-catalyzed loss of methoxyl. This could arise by the hydrolysis of methyl acetal linkages or by the solubilization of methoxyl-bearing components which are not extracted by ether. The lignin extracted by the 1-hour treatment was of a light tan color and its methoxyl content of 16.1% agrees with that reported by Björkman (6) for a sample of spruce milled wood lignin whose methoxyl content of 15.8%, after correction for 1.9% hydrolyzable carbohydrates, becomes 16.1%. A similar 1-hour preparation analyzed for carbon, 64.6; hydrogen, 5.55%; results, which again agree closely with the elemental analysis of other extracted lignins.

The steady decrease, with time of extraction, of the methoxyl content of both the isolated lignin and the corresponding ether extracts may be explained as follows. Either the protolignin is non-homogeneous, at least with respect to its ease of extraction, and the higher percentage methoxyl components are most readily liberated and solubilized (e.g., terminal units), or the isolated "lignin" fraction contains increasingly larger relative amounts of carbohydrate fragments. This latter situation could arise as the result of the direct isolation of such lignin–carbohydrate portions pre-existing in the wood, or as a result of secondary condensations between solubilized lignin and carbohydrate fragments.

It was felt that some information might be obtained regarding the homogeneity of the protolignin if a stepwise isolation were conducted and the lignin products examined at each stage. To this end the residual pulp from the 1-hour extraction procedure (25 g wood meal) was treated under the same experimental conditions for a further 1½ hours and the solubilized lignin and ether extracts obtained. This was repeated again on the second pulp residue. The lignin yields with methoxyl content given in brackets, obtained by the successive extraction periods of 1, 1.5, and 1.5 hours, were 2.25 g (16.1%), 0.684 g

(14.85%), and 0.514 g (14.5%). The corresponding ether extracts were 0.774 g (14.9%), 0.338 g (8.45%), and 0.21 g (4.62%). There is a considerable decrease in the total available lignin products as compared to those obtained by either the one-step 2.5 hours or the one-step 4.0 hours extraction. The chemical nature of these products isolated by the successive stepwise method varied considerably, indicating a non-homogeneity of the lignin substance. It must be pointed out that each wood residue was dried first in the air then in a vacuum desiccator over phosphorus pentoxide, and it is conceivable that during this time oxidation or condensation occurs which decreases the ease of subsequent isolation.

The ready availability, light tan color, high methoxyl content, and solubility in dioxane–water (9:1) of the lignin isolated by the 1-hour treatment was considered as sufficient indication that this material would prove suitable for extended chemical studies. Thus, studies could be made on the effect of increasing times of acidolysis on the establishment of carbon–methyl groups by rearrangement, and on the liberation of free phenolic hydroxyl groupings. For this purpose solvent-extracted wood meal (300 g) was extracted, as before, for a 1-hour period. The resulting lignin weighed 31.2 g (37.8% of the Klason lignin) and analyzed for 15.53% methoxyl. The ether extract yielded a dark colored oil fraction, 7.92 g (9.6% of the Klason lignin) which was not studied further.

Samples of this dioxane–water lignin were subsequently refluxed further under similar conditions for periods of 3, 11, 23, and 47 hours. The resulting reaction products were studied as before, the lignin recovered by precipitation into 1% sodium sulphate, and the ether-soluble oils extracted from the aqueous filtrate. The results of these treatments are given in Table III.

TABLE III

Acidolysis of isolated dioxane–water lignins[a]

Run	Sample (g)	Reflux (hours)	Lignin recovered		Ether extract		Methoxyl recovery (%)
			Weight (g)	OCH_3 (%)	Weight (g)	OCH_3 (%)	
A	4.0017	3	3.1432	16.2	0.394	17.52	93.0
B	4.0255	11	3.0178	16.4	0.473	16.75	91.5
C	4.0024	23	3.1103	16.19	0.457	18.4	94.5
D	4.003	47	3.0599	16.06	0.426	16.7	90.5

[a]Reaction medium: dioxane–water (9:1) (100 ml); 0.2 *N* HCl.

The consistently high methoxyl content of the recovered lignins indicates the stability of this grouping to these reaction conditions. This fact, together with the close similarity in the amounts of the ether extracts, suggests a rapid release of these lower molecular weight fragments from this lignin. Support is thereby also given to the belief that the decrease in methoxyl content of both the isolated lignin and the ether-soluble extracts, with increasing time of acidolysis of the original wood (see Table II), is a result of the simultaneous isolation of lower methoxyl content portions. A progressive darkening in color of the isolated lignins from run A through D indicates a distinct chemical change which, however, did not result in a change of the methoxyl content. The analytical results showing the increasing content of both carbon–methyl and of free phenolic hydroxyl groups with increased time of acidolysis have been reported and their significance to the chemistry of spruce lignin discussed (9). It is obvious that extensive rearrangements or other structural changes were occurring as a result of the prolonged treatment.

B. ISOLATION OF LIGNIN FROM ASPEN WOOD

The method of lignin isolation described above offered a simple but rapid means of obtaining, in good yields, a light, tan-colored material suitable for further extensive chemical studies. The method was then applied to a typical angiosperm, *Populus tremuloides*. The effects of time of extraction on the yields of the precipitated lignin and the ether-soluble oils along with their respective methoxyl contents are given in Table IV.

TABLE IV

Effect of reflux time on isolation of aspen lignin[a]

Reflux time (hours)	Residual pulp		Lignin recovered[b]					Ether extract			Total OCH_3 recovery (%)
			Weight			Methoxyl		Weight		OCH_3 (%)	
	Recovery (%)	OCH_3 (%)	A (g)	B (g)	Total (% K.L.)	A (%)	B (%)	(g)	(% K.L.)		
0.5	80.5	2.63	1.75	0.17	42.2	21.0	15.9	0.34	7.5	19.1	77.8
1.0	73.0	1.87	2.36	0.11	54.3	21.5	12.8	0.54	11.9	18.7	75.0
2.5	64.0	0.77	2.71	0.42	68.8	20.8	15.6	0.39[c]	8.6	11.5	62.4[c]
4.0	61.2	0.30	3.22	0.01	71.0	20.3	12.9	0.99	21.8	15.8	66.8
8.0	56.9	0.32	3.34	0.13	76.3	19.5	15.6	1.41	31.0	14.4	71.5
48.0	46.5	0.69	4.85	0.02	107.	16.3	—	1.26	27.7	12.4	80.0

[a]Reaction conditions: extracted wood meal (25 g); dioxane–water (9:1) (200 ml); 0.2 *N* HCl; reflux temperature, 90–94° C, under nitrogen.

[b]Lignin A refers to that fraction obtained from the neutralized filtrate; lignin B to that fraction obtained from $NaHCO_3$ layer.

[c]Unknown mechanical loss during evaporation.

One of the striking features of this extraction of aspen wood meal is the consistently low recovery of methoxyl as compared to that obtained from spruce wood by a similar treatment. Two possible reasons for this poor recovery may be suggested; either a significant proportion of the original methoxyl is present in an acid labile form, e.g., acetal linkage, or it is associated with readily hydrolyzable carbohydrate fractions which remain unrecovered in the aqueous residue. As high as 15% of the methoxyl of aspen wood has been reported (10) to be associated with the holocellulose.

The steady decrease in the methoxyl content of the isolated lignins and of the ether extracts with times of extraction from 0.5 to 48 hours follows a pattern similar to that found for spruce and may be likewise explained. The high (21%) methoxyl content of the lignin isolated after ½-hour or 1-hour treatments is in general agreement with the several values reported by Brauns (1) ranging from 20.4 to 20.9% and slightly higher than the 19.4% reported for native aspen lignin (11). The results presented in Table IV suggest that as a result of extended acidic treatment secondary reactions occur involving the isolated lignin and residual carbohydrate components. The significantly increasing methoxyl content of the pulps after longer than 4 hours' extraction time indicates a recombination of methoxyl-bearing components and pulp residues.

The characteristic reaction of hardwood lignin whereby it may be oxidized by hot alkaline nitrobenzene solution to produce vanillin and syringaldehyde was applied to the isolated lignins recorded in Table IV. These results are given in Table V.

It is very significant that even after only a ½-hour acidolysis treatment, the yields of vanillin and syringaldehyde have been markedly decreased over those obtainable using wood meal alone. No results were obtained respecting the aldehyde yields of the ether extract, but since it represented only 7.5% of the total lignin, the possible aldehyde yields would be less than this value. The combined yields of vanillin and syringaldehyde from the isolated lignin and from the residual pulp of the ½-hour extraction procedure

TABLE V

The alkaline nitrobenzene oxidation of isolated aspen lignins

	Yields of aldehydes[a]							
Reflux time (hours)	0[b,c]	0.5	1.0	2.5	4.0	8.0	48	0.5[c] (Wood residue)
Vanillin	17.0	8.2	8.4	6.2	5.7	5.0	4.6	1.39
	14.1	8.4	10.5	6.3	4.1	4.8	3.6	1.46
	14.9	7.8	7.3	6.6	4.4	4.1	3.3	1.31
	19.5							
Mean	16.6	8.1	8.7	6.4	4.7	4.6	3.8	1.39
Syringaldehyde	33.7	24.0	24.8	18.3	15.3	11.2	6.4	1.89
	32.6	22.0	25.5	16.9	13.4	10.5	5.8	2.20
	33.0	23.7	21.4	18.1	12.6	9.9	5.1	2.11
	36.1							
Mean	33.9	23.2	23.9	17.8	13.8	10.5	5.8	2.07
Total vanillin and syringaldehyde	50.5	31.3	32.6	24.2	18.5	15.1	9.6	3.46
Ratio S/V	2.0	2.9	3.0	2.8	2.9	2.3	1.5	1.5

[a]Reported as percentage by weight of the isolated lignin.
[b]Solvent-extracted wood meal.
[c]Reported as percentage by weight of the original Klason lignin.

amounted to only 9.49 and 25.3%, as compared to yields of 16.6 and 33.9% respectively obtained from the wood meal itself and calculated as percentage of the Klason lignin. This marked difference suggests a very rapid change in chemical structure, under the conditions of the acidolysis, into a form which no longer is oxidized to the phenolic aldehydes. A strikingly similar result was observed previously by Kavanagh and Pepper (12), who showed that if similar wood meals were subjected to a 2.5-hour pretreatment with 8% sodium hydroxide, then on subsequent oxidation with nitrobenzene yields of vanillin and syringaldehyde were only 9.65 and 22.6% respectively. It seems clear that as a result of either an acid- or base-catalyzed reaction, structural changes in the lignin occur rapidly either prior to, during, or after solution of the lignin fraction.

The methoxyl content of aspen lignin may be considered to arise from the methoxyl groups associated with the guaiacyl and syringyl nuclei of the lignin substance. If a typical guaiacyl-containing unit be represented by $C_{10}H_{12}O_4$ and a typical syringyl-containing unit by $C_{11}H_{14}O_5$, a ratio of these two units of close to 2:1 respectively would be equivalent to a combined methoxyl content of 21% as found for the least modified isolated lignin (see Table IV). As may be seen from Table V the actual ratios of vanillin to syringaldehyde as obtained by the alkaline nitrobenzene oxidations are all (except in the 48-hour experiment) close to 1:3. Since neither vanillin nor syringaldehyde is lost to any appreciable extent by this treatment (12), the inverse ratio and high relative yields of syringaldehyde may be explained as follows. Under the conditions of the reaction a secondary condensation occurs involving the reactive 5-position of the 1-substituted guaiacyl nuclei giving rise to products that no longer can be oxidized to vanillin. No such secondary reaction is possible for the fractions composed of syringyl nuclei.

The increasing carbon–methyl content of the isolated spruce wood lignin with increasing time of subsequent further acidolysis treatment has already been reported (9). The carbon–methyl/methoxyl ratio increased from 0.04 to 0.20 as a result of a 48-hour

acidolysis treatment. Similarly, for the lignin isolated from aspen wood the carbon–methyl/methoxyl ratio was shown to increase with increasing times of acidolysis during isolation. After 0.5, 1.0, 2.5, 4.0, 8.0, and 48.0 hours of acidolysis, the average carbon–methyl/methoxyl ratio was 0.13, 0.10, 0.11, 0.15, 0.22, and 0.29 respectively.

These results again indicate the rearrangements that readily occur intramolecularly in isolated lignins. They emphasize too the requirement of short times of extraction in order to obtain a representative lignin fraction. Earlier workers (2) had shown that for maple negligible amounts of carbon–methyl groups existed in the whole wood other than those derivable from the readily hydrolyzable acetate groupings.

The application of this procedure of lignin isolation to both spruce and aspen woods gives rise in good yields to a readily obtained product, which, on preliminary examination, appears to be only moderately changed from protolignin. In comparison it appears that aspen wood lignin is isolated rather more easily than that from spruce wood. It appears too, that there is evidence in the former case for an initial rapid extraction of about two-thirds of the lignin followed by a slower rate of extraction of the remainder. There is no similar inflection in the rate of lignin isolated from spruce. This effect may be associated with the proved dinuclear character of the hard wood lignins as compared to the greater homogeneity of the softwood lignins. This suggested greater ease of cleavage, and subsequent dissolution of fragments with syringyl-type nuclei is supported by the evidence presented regarding the relative yields of aldehydes obtained by oxidation.

EXPERIMENTAL

Preparation and Analysis of Wood Meal

Spruce wood.—Swedish spruce wood meal was extracted continuously with a mixture of ethanol–benzene (1:1) for 53 hours, air-dried, and finally dried to constant weight in a vacuum desiccator over phosphorus pentoxide. Anal: Klason lignin, 27.55%; methoxyl, 4.85%.

Aspen wood.—Native Saskatchewan aspen (*Populus Tremuloides*) sapwood, 20 mesh, was extracted with ethanol–benzene (1:1) for 45 hours, air-dried, and finally dried to constant weight over phosphorus pentoxide. Anal.: Klason lignin, 18.2%; methoxyl, 5.13%.

Solvent.—The dioxane was purified according to the procedure of Fieser (13).

General Procedure for Lignin Isolation

A procedure typical of that used for all acidolysis treatments is as follows. Pre-extracted wood meal (25 g) was placed in a 2-liter, 3-necked flask fitted with a reflux condenser, a nitrogen bubbler, and a dropping funnel. The flask was evacuated at the water aspirator (10–15 minutes), the connection to the pump closed, and the solvent system (200 ml of dioxane–water (9:1) containing 1.46 g dry HCl gas) added slowly from the dropping funnel. The reaction mixture was heated using a heating mantle and refluxed gently for varying periods of time of 0.5, 1.0, 2.5, 4.0, 8.0, and 48 hours under a nitrogen atmosphere. For the experiments using aspen wood the reaction mixture was stirred using a magnetic stirrer. The reaction mixture was allowed to cool, filtered whilst blanketed with nitrogen, and the residue washed on the filter with a further 50 ml of the same solvent. The residual pulp was dried to constant weight and analyzed for methoxyl content.

The filtrate was neutralized with excess sodium bicarbonate and allowed to stand overnight. The liquid layer was concentrated under reduced pressure, using a nitrogen leak, to a thick syrupy consistency, dissolved in ca. 30 ml of the solvent, and forced

under pressure (syringe bulb) in a fine stream under the surface of 250 ml of a 1% Na_2SO_4 solution. The precipitated lignin was separated by centrifugation and decantation, washed thoroughly with water, and centrifuged three times more, and finally dried to constant weight in a vacuum desiccator over P_2O_5. In the case of the aspen wood experiments, the sodium bicarbonate sludge layer was dissolved in a large excess of water (60 ml) and acidified with hydrochloric acid. The lignin thus precipitated is referred to as lignin B in Table IV.

Those lignins isolated by the short periods of reflux (0.5–1.0 hours) were light tan-colored powders, but the color darkened as the time of reflux increased. These lignins were all slightly hygroscopic, highly susceptible to static electricity when dry, soluble in pure dioxane or dioxane containing a few per cent water, and soluble in glacial acetic acid and sodium hydroxide but only slightly soluble in ether and carbon tetrachloride.

The alkaline nitrobenzene oxidations were conducted according to the procedure of Stone and Blundell (14).

The carbon–methyl analyses were determined according to the procedure outlined by Smith and Shriner (15).

ACKNOWLEDGMENTS

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HYDRONIUM ION ABSORPTION IN THE REGION 1.7 μ[1]

W. J. Biermann and J. B. Gilmour

ABSTRACT

Optical absorption of the hydronium ion in the region 1.7 μ was measured in solutions of nitric acid and perchloric acid in the concentration range 0.01 to 4.0 moles per liter. Above 0.1 molar the absorption did not follow Beer's Law, being smaller than predicted from the low concentration behavior. This enhanced transparency is attributed to a "negative absorption" band, associated with the change in solvent structure, found in this spectral region.

INTRODUCTION

In an attempt to establish relationships between the thermochemical properties of aqueous solutions of strong acids and the structures of these solutions, the degree of dissociation of the acid is an indispensable quantity. The limited information presently available has been based, for the most part, on observations of the optical absorption or Raman spectra of undissociated molecules and the anions produced in dissociation (1, 6, 7, 9, 10, 12). The degree of dissociation of a few oxyacids, notably nitric and perchloric acids, seems to be reliably established over a wide concentration range, but these methods are not applicable to binary strong acids.

While casting about for alternate methods of studying the dissociation of strong acids in aqueous solutions, we observed the near infrared absorption spectra of a number of aqueous solutions of strong acids (2). In all cases, these spectra showed a strong absorption band centered in the region of 1.7 μ (5800 cm^{-1}). It appeared reasonable to classify this as an harmonic of a fundamental vibrational frequency of the hydronium ion. Very shortly thereafter, Giguère and Falk (5) reported broad absorption peaks for the hydronium ion at 2900 cm^{-1} and 3300 cm^{-1}.

A study of this absorption band over a range of concentrations was undertaken, primarily to determine the applicability of Beer's Law. If Beer's Law were obeyed, a useful method would be available for the determination of the degree of dissociation of acids in water. Nitric acid and perchloric acid solutions were chosen because the hydronium ion concentrations of these can be calculated with some degree of confidence from existing data.

EXPERIMENTAL

Nitric and perchloric acid solutions were prepared by diluting concentrated reagent grade chemicals with conductivity water. The diluted solutions were analyzed by titration with carbonate-free sodium hydroxide solutions, using bromcresol purple as indicator. The percentages of light transmitted by the diluted solutions were measured on a Beckmann DK-II spectrophotometer, using 1.0-cm Corex cells at room temperature. Conventional procedures were used to insure temperature similarity between the solution and the water-filled reference cell, to correct for inequalities of cell length, and to minimize the chance of gross error by a suitable schedule of repetition of observations.

The experimental results are summarized in Tables I and II, which give the average absorbancy ($\log_{10} I_0/I$) and the wavelength of the maximum of the absorption peak for a range of concentrations of nitric acid and perchloric acid from 0.01 to 4.0 molar. All the absorbancy values were measured at the wavelength of maximum absorption. Figure 1

[1]*Manuscript received March 16, 1959.*
Contribution from the Department of Chemistry, University of Manitoba, Winnipeg, Manitoba.

TABLE I

Absorbancy data for aqueous perchloric acid solutions

Concentration, moles $HClO_4$/liter	Absorbancy, $\log_{10} I_0/I$	Wavelength (μ) of max. absorption
0.009706	0.0067	
0.01948	0.0156	
0.02925	0.0252	
0.03912	0.0313	1.730
0.04836	0.0383	1.738
0.05795	0.0453	1.738
0.06937	0.0550	1.741
0.07754	0.0696	1.736
0.09733	0.0775	1.736
0.1957	0.152	1.738
0.2936	0.225	1.738
0.6303	0.458	1.738
0.7305	0.526	1.735
0.9358	0.650	1.732
1.233	0.823	1.727
1.562	0.983	1.723
1.967	1.153	1.715
2.423	1.286	1.712
2.933	1.385	1.708
3.859	1.477	1.700

TABLE II

Absorbancy data for nitric acid solutions

Concentration, moles HNO_3/liter	Absorbancy, $\log_{10} I_0/I$	Wavelength (μ) of max. absorption
0.00928	0.0073	1.735
0.01878	0.0161	1.735
0.04762	0.0417	1.735
0.09413	0.0834	1.734
0.1998	0.173	1.732
0.3839	0.323	1.734
0.5645	0.460	1.731
0.7433	0.587	1.730
0.9534	0.730	1.726
1.171	0.863	1.721
1.581	1.093	1.714
2.005	1.264	1.710
2.492	1.407	1.705
3.044	1.507	1.697
3.909	1.576	1.696

is a graphical presentation of the absorbancy, plotted against concentration. The solid lines are extensions of the limiting slopes and, since both of these acids are substantially completely dissociated in the concentration range studied, are approximately the loci which would be anticipated if the absorption followed Beer's Law. Figure 2 shows the low concentration absorbancy versus concentration plot, in which Beer's Law is obeyed within the accuracy of observation.

DISCUSSION

That the phenomenon being observed is more complex than a simple absorption of light by H_3O^+ is shown by four types of behavior inconsistent with the simple picture:

1. Absorbancy falls off too rapidly with concentration. If the experimental results are used to compute degrees of dissociation on the assumption that Beer's Law is applicable, these are much lower than the values consistently obtained by other methods.

2. The wavelength of the peak maximum shifts to a lower value as the concentration increases.

3. Nitric acid appears to be "stronger" than perchloric acid, whereas all other investigations have shown perchloric acid to be the stronger.

4. The limiting value of the extinction coefficient differs between nitric and perchloric acids.

The shift in the peak maximum is a particularly strong indication that the entity being observed does not retain its physical structure throughout the concentration range.

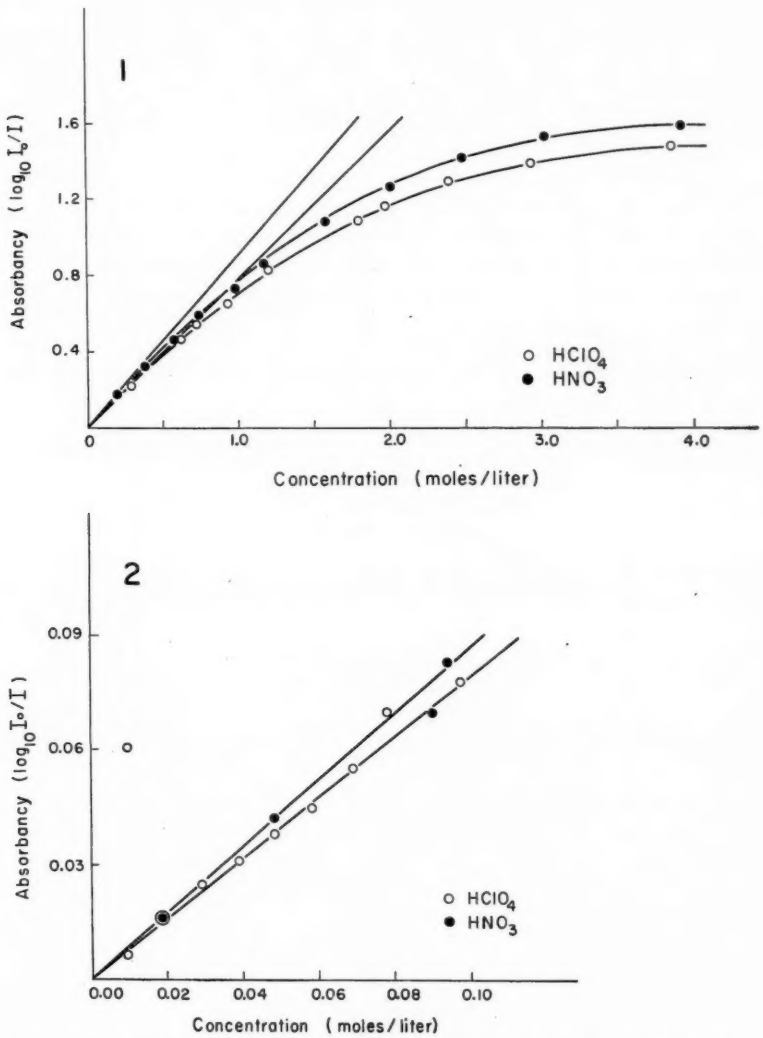

FIG. 1. Absorbancy of aqueous solutions of nitric and perchloric acids in the region 1.7 μ.
FIG. 2. Absorbancy of nitric and perchloric acid solutions at low concentrations.

It is quite certain that the H_3O^+ ion, which has three hydrogen atoms available for bonding to oxygen atoms and a positive charge, is connected by hydrogen bonding to the surrounding water molecules. Raman studies by Cross, Burnham, and Leighton (4) have shown that at low temperature water has a fourfold co-ordination structure, but above 26° C the twofold co-ordination structure predominates. The structure of course is a dynamic one; over a long range there would appear to be repetition of units, but nevertheless there is a short range order. Hence, the co-ordination or hydration sphere of the H_3O^+ ion would include not free water molecules but a structure at least similar to that of water itself, and would therefore be subject to any change in the solvent, which would be reflected by a change in the co-ordination sphere of the hydronium ion.

If this picture is close to the true model of a dissociated acid in water, one can expect a change in the nature of the $H_3O^+.nH_2O$ hydrate with concentration. At higher concentrations, hydronium ions would compete for available water units in order to form co-ordination spheres. Once these co-ordination spheres are formed, they would be subject to any change in the structure of the solvent.

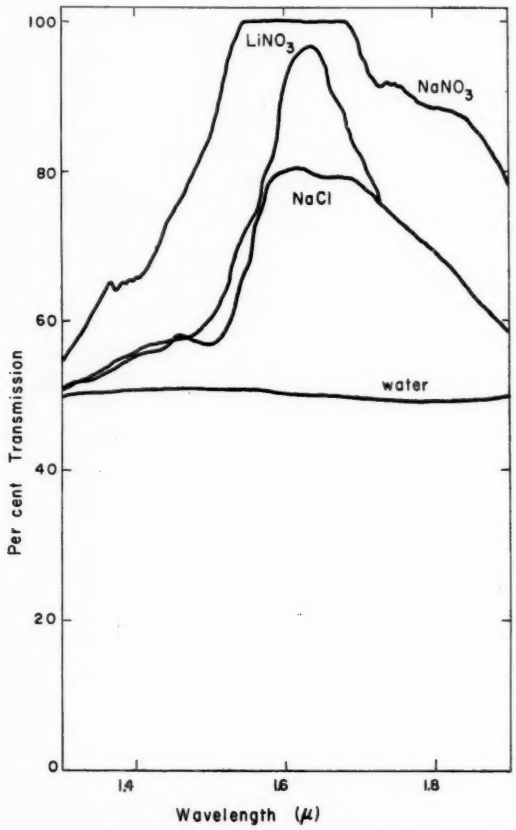

FIG. 3. Optical transmission of some salt solutions relative to the transmission of water in the region 1.7 μ.

It is well known that the association of water is disturbed by an electrolyte. Bernal and Fowler (3) first suggested that electrolyte ions cause a rearrangement of the structure of liquid water. Leighton and Burnham (8) showed that zinc chloride, when dissolved in water, causes a shift in the short frequency component of a main Raman band. Using the X-ray diffraction curves of lithium chloride, sodium chloride, and potassium chloride in aqueous solution at 15° C, Stewart (11) demonstrated that with increasing ionic concentration, the amount of fourfold co-ordination of water is lessened.

The absorbancy values observed above 1 molar are lower than would be anticipated from available dissociation data. Introduction of ions would undoubtedly cause some measure of distortion of the structure of water, probably through orientation of water dipoles, especially in the case of a small ion. The water in an ionic solution might then absorb less light than pure water at the same wavelength. (One can conveniently call this "negative absorption".) The existence of some such negative absorbance mechanism, superimposed on the position absorbance of the hydronium ion, offers a facile explanation for the low absorbancies found for nitric and perchloric acids.

If such a negative absorption is caused by the introduction of hydronium ions, it should also be caused by introduction of any small positively charged ions which are hydrated, such as sodium or lithium ions. Since they will have no positive absorption in this region, solutions containing sodium or lithium ions should be more transparent than water in the spectral region 1.7 μ. Figure 3 shows shapes of curves which resulted when the absorbancies of lithium nitrate, sodium nitrate, and sodium chloride solutions were compared to water. As predicted, all of the solutions gave negative absorption in the region of the absorbance peak of the acids. These solutions were all approximately 1 molar.

It is planned to examine the applicability of Beer's Law to the other two absorption bands reported for the hydronium ion and to examine the "negative absorption" of a series of solutions containing small cations.

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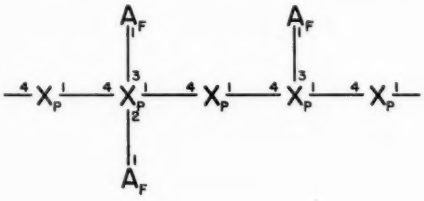
THE ARRANGEMENT OF BRANCHING IN AN ARABINO-XYLAN FROM WHEAT FLOUR[1]

CONSTANCE M. EWALD[2] AND A. S. PERLIN

ABSTRACT

The manner in which L-arabinofuranose branches are arranged along the xylan chain of the pentosans has been examined. The approach used was based on the fact that D-xylose units engaged in branching are resistant to periodate oxidation whereas other sugar residues are readily attacked. Selective degradation of oxidized portions of the polymer with phenylhydrazine or sulphurous acid enabled the isolation of fragments which corresponded to branch points in the original pentosans. D-Xylose and xylobiose were the major products obtained, and xylotriose a minor product. The results indicate that L-arabinose branches of the polysaccharide occur sometimes on isolated D-xylose residues, sometimes on two adjacent D-xylose units, less frequently on three, but not on four, five, etc., consecutive D-xylose residues along the chain.

A water-soluble polysaccharide fraction isolated from wheat flour has been shown to contain a group of closely related pentosans composed of D-xylose and L-arabinose (1, 2). Structure I (A_F = L-arabinofuranosyl; X_P = D-xylopyranosyl) was suggested as an average representation of these pentosans (2), a formulation which has received support in more recent studies (3). Pentosans from a variety of plant sources appear to have a similar type of structure, differing mainly in the relative proportion of the two pentoses or in containing D-glucuronic acid (or a methyl ether of it) as a third component sugar



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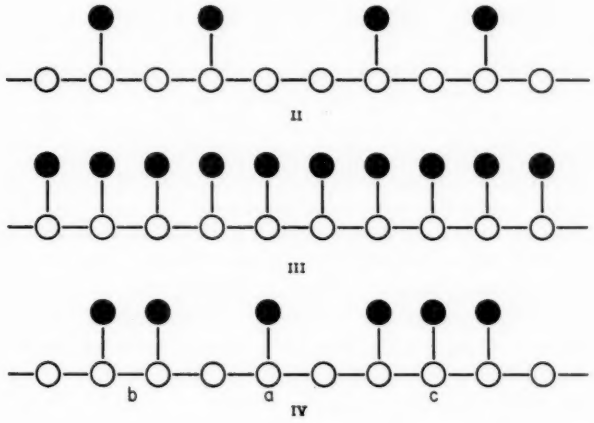
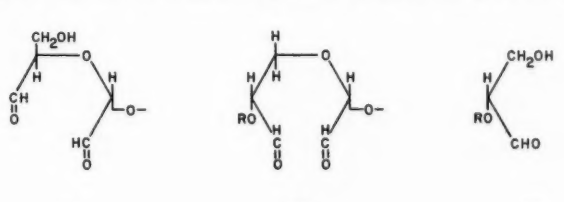
(e.g., 4, 5, 6, 7, 8 and references therein). Major structural features are a linear chain of β-D-xylopyranose units joined by (1 → 4)-linkages, and L-arabinofuranose (or uronic acid) end groups, which, in at least some of the polysaccharides (2, 4, 7), are attached directly by (1 → 2)- or (1 → 3)-linkages to the xylan chain. The available data do not define how the branches in these polysaccharides are arranged, and are consistent with a variety of sequences. Thus, branching may be uniform throughout (II white circles = D-xylopyranosyl; dark circles = L-arabinofuranosyl), in some molecules the incidence of side chains very high (III), or a mixture of arrangements (IV), may be found. The current paper deals with attempts to obtain more definitive information about the mode of branching in the wheat flour pentosans.*

[1]*Manuscript received April 20, 1959.*
Contribution from the National Research Council of Canada, Prairie Regional Laboratory, Saskatoon, Saskatchewan. Presented at the 41st Annual Conference, The Chemical Institute of Canada, Toronto, May 26–28, 1958.
Issued as N.R.C. No. 5262 and as Paper No. 261 on the Uses of Plant Products.
[2]*Research assistant, 1953.*
**Detailed information about the arrangement of branching in complex polysaccharides is generally lacking. The chain length of branches in polymers such as glycogen or amylopectin, for example, must be regarded at present as an average value rather than an accurate representation of the size of each branch.*



In devising an approach to this problem the following considerations were made. Treatment of the pentosans with periodate promotes oxidation of the L-arabinose units and D-xylose units which do not constitute branch points. Selective removal of oxidized residues and isolation of unoxidized portions of the molecule as intact fragments should then permit a distinction between II, III, IV, etc. According to this scheme, for example, structure II would afford D-xylose, III a polymeric xylan, and structure IV mono-, di-, and tri-saccharides.

A means for degrading dialdehydes* from periodate oxidation through reaction with phenylhydrazine acetate was developed by Barry (9). The method has been used effectively in examining the fine structure of several polysaccharides which are oxidized partially by periodate (9, 10, 11, 12, 13, 14) facilitating the removal of oxidized portions of the polymers. With a dialdehyde such as V the reagent cleaves the oxygen-bridge and forms glyoxal bis(phenylhydrazone) and triose phenylosazone. It was to be expected, therefore, that the Barry reaction would remove oxidized L-arabinofuranose units (the L-isomer of V) from the oxidized pentosans. Similarly, a dialdehyde (VI) adjacent to a second dialdehyde residue (R) yields osazones of glyoxal and glycerose. However, when R is an unoxidized unit the dialdehyde may yield a hydrazone of VII (R = glycosyl) in addition to glyoxal bis(phenylhydrazone), or the glycosidic bond may be cleaved giving triose phenylosazone and a sugar, the latter being converted in turn to an osazone. These reactions were expected to occur with disruption of the partially oxidized xylan chain.



V VI VII

*The dialdehydes may exist in equilibrium with several cyclic modifications (Michell, J. H. and Purves, C. B. J. Am. Chem. Soc. **64**, 589 (1942)). For a recent discussion of these structural types see Goldstein, I. J., Lewis, B. A., and Smith, F. J. Am. Chem. Soc. **80**, 939 (1958).

Depending on the arrangement of branches in the polymer, it was evident that the Barry degradation could yield a complex mixture of products. As osazones, the unoxidized fragments might be especially difficult to separate and characterize, particularly since they would represent as a maximum only about 30% of the original polysaccharide (2). Alternatively, by avoiding use of excess phenylhydrazine, it was found that only a portion of the liberated sugars are converted into osazones and hence could be examined by conventional sugar techniques. In this modification of Barry's procedure, low molecular weight osazones were readily separated from other components of the reaction mixture, and the water-soluble fraction was treated with benzaldehyde to decompose hydrazones (15) which might have been formed. The aqueous solution then afforded in low yield approximately equal amounts of D-xylose and 4-*O*-β-D-xylopyranosyl-D-xylose (xylobiose) as the major products. Xylotriose (16), characterized tentatively, was a minor product, but oligosaccharides of higher molecular weight were not found.*

With excess phenylhydrazine acetate, the oxidized polysaccharide was degraded extensively to low molecular weight fragments and no product corresponding to a xylan was isolated. This finding made it unlikely, therefore, that a substantial proportion of the L-arabinose units are to be found in a densely packed arrangement as in III. Chromatographic examination of the reaction mixture indicated the presence of xylosazone, xylobiosazone, and only traces of higher molecular weight products, in addition to a very large proportion of glyoxal and glyceraldehyde osazones. A partial separation of these products was achieved by column chromatography on silicic acid – Celite (17).

Another procedure examined briefly as a possible means for selectively degrading the periodate-oxidized pentosans employed graded hydrolysis with sulphurous acid. Periodate dialdehydes are remarkably resistant to hydrolysis with mineral acids (18, 19), but are smoothly hydrolyzed by sulphurous acid (20). Progressive gentle hydrolysis of the oxidized pentosans with a saturated solution of sulphur dioxide produced xylose, xylobiose, and a trace of xylotriose (followed chromatographically in small-scale experiments). A small proportion of arabinose which had escaped, or was resistant to, oxidation by periodate (2) was also found on the chromatograms. The two oligosaccharides were hydrolyzed in turn by continued treatment, but no other oligosaccharides were detected.

The data obtained by use of these different procedures are consistent, and indicate that L-arabinose residues in the wheat flour pentosans are linked to isolated D-xylose units (IV*a*), or to two consecutive D-xylose units (IV*b*); occasionally, branching appears to involve three consecutive D-xylose units (IV*c*). It is possible, however, that the pentosans contain branches arranged in yet other ways which have not been detected by the methods used.

EXPERIMENTAL

Water-soluble wheat flour pentosans were prepared from commercial unbleached flours by the acetylation procedure described earlier (1) or by the method of Simpson (21).

Paper chromatography was carried out on Whatman No. 1 paper. Circular chromatograms (22) were used for osazones, the solvent being toluene–ethanol–water (270:30:1) (12) and variations of this mixture to speed up or slow development.

Pentosan was determined by the orcinol method (23).

Preparation of Periodate-oxidized Pentosans

The pentosans (10 g) were moistened with ethanol, pasted in water, and the solution was adjusted to a volume of 700 ml with water. Sodium periodate (17 g) in water (300 ml)

In a preliminary report of this work (Ewald, C. M. and Perlin A. S. Chem. in Can. **10 (No. 4), 62 (1958)) only D-xylose and xylobiose were listed as relevant degradation products.*

was added and the solution stored at 16° in the dark for 100 hours. Excess periodate was reduced with ethylene glycol, the solution was concentrated *in vacuo* at 40–45° to about one-third volume, and acetic acid added with stirring until a copious precipitate formed. The precipitate, which was insoluble in water, was filtered off and washed with water until it gave a negative starch iodide test, then washed with methanol, and dried. Weight 9.5 g. The dialdehyde content of the product, measured potentiometrically by the hydroxylamine method (24) was 0.67 mole per mole, in good agreement with the measured periodate uptake of 0.65–0.70 mole per mole (2). Pentosan content, 33%.

Partial Degradation of Oxidized Pentosans with Phenylhydrazine Acetate

Oxidized pentosans (7 g) in 45% ethanol (650 ml) were heated on the steam bath together with phenylhydrazine (20 ml) and acetic acid (20 ml) for 1.5 hours. The clear solution obtained was concentrated *in vacuo* at 45–50° to a thick slurry which was taken up in water and extracted exhaustively with ether. Paper chromatographic examination indicated that the ether extract contained osazones mainly of glyoxal and glyceraldehyde and of xylose in low proportion, and that the water extract contained mainly xylose, xylobiose in about equal proportion, and a trace of xylotriose together with dark material which streaked heavily on the paper. Two other trace products detected in the water extract (R_{xylose} 0.7 and 0.4) were eluted from paper chromatograms in one run and found by acid hydrolysis to contain xylose and arabinose.

Benzaldehyde (6 ml) and benzoic acid (0.5 g) in ethanol (150 ml) were added to the water extract (200 ml), the solution was heated on a steam bath for 8 hours and then evaporated at 45° almost to dryness. Water was added, the solution was extracted with chloroform (three times), then exhaustively with ether, and concentrated to dryness. Weight 1.73 g. Extraction of the residue with hot ethanol and evaporation of the ethanol afforded a yellow powder (0.83 g) a portion of which (0.65 g) was transferred to a column (2×20 cm) of coconut charcoal (25). Water (200 ml) eluted a dark brown solution which contained some xylose and xylobiose. Gradient elution (26) of the column with aqueous ethanol up to a concentration of 35% afforded a series of fractions.

The first fraction (0.10 g), $[\alpha]_D^{23}$ +13° (*c*, 2, water), contained mainly D-xylose, which crystallized from methanol–ethanol m.p. 141–143°, undepressed; the X-ray diffraction pattern was indistinguishable from that of D-xylose. The derived (2,5-dichlorophenyl)-hydrazone had m.p. 133–136°, undepressed by admixture with D-xylose(2,5-dichlorophenyl)hydrazone (27).

A second fraction (0.08 g), $[\alpha]_D^{23}$ −21° (*c*, 2.7, water), yielded, on acetylation with hot acetic anhydride – sodium acetate, a product having m.p. 154–156°; a mixed melt and comparison of X-ray diffraction diagrams showed that the product was 4-*O*-β-D-xylopyranosyl-β-D-xylose hexaacetate (16). Calc. for $C_{22}H_{30}O_{15}$: C, 49.44%; H, 5.66%. Found: C, 49.62%; H, 5.91%.

At higher alcohol concentrations, a third product was obtained (0.02 g), $[\alpha]_D^{23}$ −44° (*c*, 2, water). On a paper chromatogram it corresponded to xylotriose but appeared to be admixed with a small proportion of another oligosaccharide(s), for, in addition to xylose, it yielded arabinose as a minor hydrolytic product. Its infrared absorption spectrum was closely similar to that of xylotriose; that of the syrupy derived acetate was indistinguishable from the infrared spectrum of hexa-*O*-acetyl-β-xylotriose. Oligosaccharides of higher molecular weight were not obtained, even by washing the column with 60% ethanol.

The water-soluble material not extracted into hot ethanol was a yellow powder (0.65 g) which contained 57% of pentosan, and hence appeared to be an incompletely degraded

polymeric residue. This material was examined further by partial hydrolysis with sulphurous acid (below).

Treatment of Oxidized Pentosans with Excess Phenylhydrazine Acetate

The procedure of Barry and Mitchell (12) was used. Oxidized pentosans (2.7 g) were taken up in 65% ethanol (115 ml), phenylhydrazine (10 ml) and acetic acid (12 ml) were added, and the mixture heated under reflux for 3.5 hours. Material which deposited on cooling (wt. 1.6 g) was readily soluble in ethanol and, after recrystallization from aqueous ethanol had m.p. 165–167°, undepressed by admixture with glyoxal bis(phenylhydrazone). Calc. for $C_{14}H_{14}N_4$: C, 70.56%; H, 5.92%. Found: C, 70.87%; H, 6.03%.

The filtrate was concentrated giving a syrup, part of which was soluble in hot water. The aqueous solution was extracted exhaustively with ether, phenylhydrazine (3 ml) and acetic acid (3.5 ml) were added, it was then heated on the steam bath for 2.5 hours, and again extracted exhaustively with ether. Evaporation of the water afforded a dark syrup (0.91 g), part of which (0.40 g) was insoluble in 80% ethanol. The insoluble portion contained 43% of pentosan and the soluble material 24% of pentosan, and appeared to be incompletely degraded products.

Paper chromatographic examination of the fraction insoluble in hot water (1.5 g) indicated that it contained osazones of glyoxal and glycerose mainly, xylose, xylobiose, and slower moving components in trace amounts. Attempts to resolve this mixture by countercurrent distribution or chromatography on alumina were unsuccessful. (Two batches of alumina tested were much more retentive than the adsorbent used by Barry and Mitchell (12).) On a column of silicic acid – Celite (2:1) (17),* the compounds corresponding on a chromatogram to glyoxal and triose phenylosazones were eluted with ether, and the addition of ether containing 5% of ethanol then eluted material corresponding on a chromatogram mainly to xylosazone. Removal of the solvent afforded a solid product (0.07 g) which, after two recrystallizations from benzene, had m.p. 164–166° (decomp.), and gave an X-ray diagram indistinguishable from that of D-xylose phenylosazone. Elution with ether containing 15% of ethanol yielded a second fraction (0.09 g) which did not crystallize, but which appeared from its chromatographic mobility and infrared absorption spectrum to be mainly xylobiose phenylosazone. Higher concentrations of alcohol promoted elution of only trace quantities of other materials.

The ether extracts appeared (paper chromatograms) to contain osazones of glyoxal, triose, and xylose, and on concentration, afforded a large proportion of *N*-acetylphenylhydrazine (combined wt. 4.2 g), colorless plates, m.p. 125–127°.

Graded Hydrolysis of Periodate-oxidized Pentosans with Sulphurous Acid

An amount (0.05 g) of oxidized pentosans was suspended in water (2.5 ml) in a pressure flask (200 ml capacity), sulphur dioxide gas introduced to saturation (20), and the flask sealed. Several samples prepared in this way were heated on the steam bath for varying periods; within a few minutes the polysaccharide swelled and then dissolved. After the chosen heating interval the flasks were unsealed, most of the excess sulphur dioxide was removed with a stream of nitrogen, and the solutions were neutralized with Dowex-1 (bicarbonate form). Paper chromatographic examination indicated that most of the arabinose was liberated within 0.5 hour together with small proportions of xylose and xylobiose; at 1.5 hours xylose and xylobiose were the major products, and a trace of xylotriose was present; on further hydrolysis the spots corresponding to xylobiose and xylotriose diminished in intensity.

**The use of this adsorbent was kindly suggested by Dr. Thomas Francis.*

The partially degraded water-soluble polymer remaining from the reaction with phenylhydrazine (above), treated with sulphurous acid under the same conditions, also yielded (chromatographic evidence) xylose and xylobiose as the major products together with minor proportions of xylotriose and arabinose; oligosaccharides of higher molecular weight were not detected on the chromatograms.

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REACTION OF TRICHLOROACETONITRILE WITH PRIMARY AND SECONDARY AMINES

PART III. STRUCTURE OF AMIDINIUM CATION IN THE LIGHT OF INFRARED STUDY[1, 2]

JOHN C. GRIVAS[3] AND ALFRED TAURINS

ABSTRACT

The infrared spectra of 14 trichloro- and trifluoro-acetamidine hydrochlorides were studied. It was concluded that protonation occurs at the imino nitrogen atom of the N-substituted amidines. Both nitrogens of the amidine grouping, C(=N)N, become electron-deficient due to resonance leading to the single structure (III), regardless of which of the tautomers is present in the equilibrium mixture, and of the number and type of substituents on the amidine nitrogen atoms. These findings predestine to *failure* any attempts to isolate the two amidine tautomers, whenever amidinium salts are involved as intermediates.

INTRODUCTION

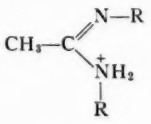
The assignment of the $-NH_3^+$, $\rangle NH_2^+$, and $\rangle NH^+$ frequencies presents a difficult problem, which has not yet been solved successfully. The infrared spectra of amine hydrohalides show many bands in the stretching region, which cannot be fully assigned. This complexity is undoubtedly due to the strong hydrogen bonding occurring in the solid phase, whereas the free vibrations are not well known since considerable difficulty is encountered in dissolving these salts in non-polar solvents.

The topic has been reviewed by Bellamy (1), by Witkop (2), and by Heacock and Marion (3). The last investigators identified the NH_2^+ deformation mode between 1620 and 1560 cm^{-1} in a series of secondary amine hydrochlorides.

Stone, Craig, and Thompson (4) were able to arrive at more definite conclusions, comparing the spectra of amine salts with those of their deuterated compounds. Thus, the $\rangle NH_2^+$ asymmetrical stretching frequency was found close to 2920 cm^{-1} and the corresponding symmetrical mode at 2780 to 2825 cm^{-1} for some secondary amine hydrochlorides. They also located the deformation frequency, $\delta(NH_2^+)$, between 1560 and 1600 cm^{-1}, in agreement with the findings of Heacock and Marion. The same authors assigned the stretching vibrations, $\nu(\rangle NH^+)$, to the band between 2330 and 2680 cm^{-1}, shown by tertiary amine hydrochlorides.

More recently Chenon and Sandorfy (5) discussed the complexity of the stretching NH^+ modes and reported the $\delta(NH_3^+)$ frequencies at 1510–1600 cm^{-1}. The strong band which appears in many cases near 2000 cm^{-1} was attributed to a combination mode between the scissoring vibration and a very anharmonic band near 400 cm^{-1}.

To our knowledge, the infrared absorption of the NH^+ vibrations of the amidinium cation has not yet been studied. However, Prevoršek (6) suggested the following structure for some N,N′-disubstituted amidine hydrochlorides, on the basis of their infrared spectra.



[1]*Manuscript received April 9, 1959.*
Contribution from the Department of Chemistry, McGill University, Montreal, Quebec, with financial assistance from the National Research Council, Ottawa, Canada.
[2]*Part II: Grivas, J. C. and Taurins, A. Can. J. Chem.* **37**, *795 (1959).*
[3]*Holder of the National Research Council Studentships, 1957–58 and 1958–59.*

EXPERIMENTAL

The infrared spectra were recorded on a Perkin–Elmer model 21 double-beam spectrophotometer equipped with a sodium chloride prism. Fluorolube T-45 mulls were used, since Nujol absorbs strongly at 2800–3000 cm^{-1}. A similar cell unit provided excellent compensation between 4000 and 1350 cm^{-1}. The results are summarized in Tables I, II, and III.

Preparation of Hydrochloride Salts

About 100 mg of freshly purified and dry amidine was dissolved in 20 ml of absolute ether and cooled to 0° C in an ice–salt bath. A stream of dry hydrogen chloride gas was passed through this solution, with continuous stirring by means of a magnetic stirrer, until no precipitation was observed. The white crystalline hydrochlorides were filtered off and dried under vacuum. Although they could not be recrystallized, since they decomposed easily, they were pure and suitable for infrared investigation.

Preparation of Deuterium Chloride Salts of N-*Methyltrifluoroacetamidine-d_2 and* N-*Methyltrichloroacetamidine-d_2*

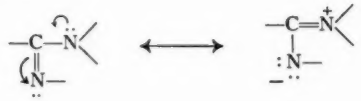
The same procedure as above was followed and gaseous deuterium chloride was used. All the operations were conducted in a dry nitrogen atmosphere.

Deuterated amidines and the free bases were prepared by known methods (7), or by procedures which will be presented in another paper. All unknown parent compounds were analyzed.

RESULTS AND DISCUSSION

Amidines are monobasic compounds, since they form monosalts with a variety of acids. A literature search revealed that very little is known with respect to the structure of the amidinium cation, which must have an important bearing on the understanding of the chemical behavior of the amidine grouping. Some authors do not draw any distinction between the two nitrogen atoms of amidines.

Theoretical considerations, however, combined with the results of this investigation by the infrared spectroscopy method, may definitely elucidate the course of protonation. Irrespective of the type and number of substituents on the nitrogen atoms, the amidine system is represented by formula (I):

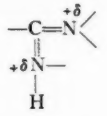


(I*a*) (I*b*)

Such a structure as shown allows for only one charged resonance form having a negative charge on the imino nitrogen and a positive charge on the other. Consequently, the imino group would be expected to accept the proton during the salt formation. Such protonation should yield a resonance hybrid receiving contributions from the two structures shown in formula (II). As a result,

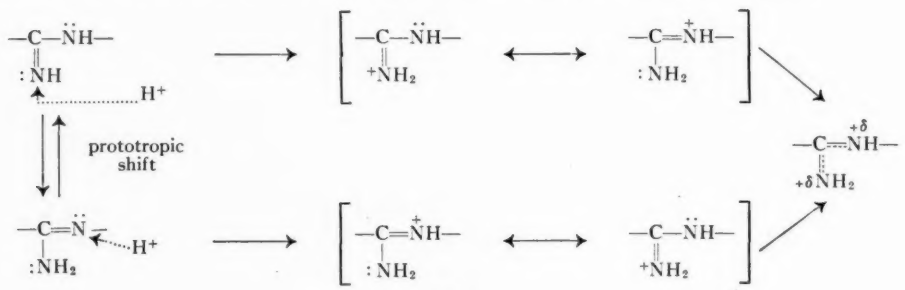
(II)

both nitrogen atoms would become electron-deficient to a degree (III), which should depend on the substituents to some extent. The decreased electron density on nitrogen atoms should prevent any further protonation.



(III)

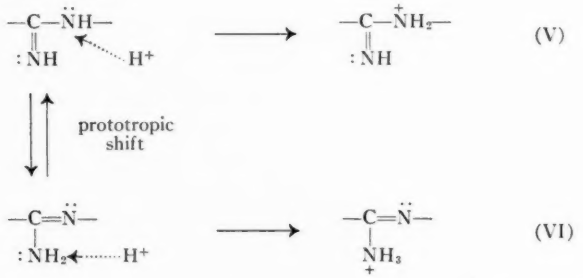
The protonation of both the plausible tautomeric forms of amidines must give one and the same compound (IV) stabilized by resonance, as outlined in the following scheme:



(IV)

This course must be valid in any case, independently of the kind of substitution, and predestines to failure any attempts to isolate the two tautomers, whenever intermediate salt formation occurs. It should be mentioned here that many such unsuccessful attempts have been made, even recently, and in all cases methods leading to salt intermediates were used.

An alternative course of protonation can be written as follows:



(V)

(VI)

It is obvious that formulae (V) and (VI) represent two relatively unstable isomers, since resonance stabilization is prevented.

The infrared spectra of the amidine hydrochlorides examined showed characteristically only the stretching vibrations of the $\overset{+}{N}H$ group and the complete absence of any absorption bands of free or bonded NH group (Tables I and II).

TABLE I

Positions of absorption maxima (cm^{-1}) in the infrared spectra of N-substituted trichloroacetamidine hydrochlorides

No.	Trichloro-acetamidine hydrochloride	M.p. (decomp.)	$\nu(\overset{+}{\underset{}{\rangle}}\!\!\overset{+}{N}H)$		and	$\nu(=\overset{+}{N}H_2)$†		$\nu(C=\overset{+}{N})$	$\delta(=\overset{+}{N}H_2)$	$\delta(\overset{+}{N}H)$
1	N-Methyl-	229°	3100sh,	*2930vs*,*		2800sh,	2300w	1680vs	1620m	1500m
2	N-Ethyl-	224–225°	3060sh,	*2950vs*,*		2800sh,	2340w	1687vs	1640m	1520s
3	N,N-Dimethyl-	175–176°	2970sh,	2910sh,		*2860vs*,*	2340w	1617vs	1530s	None
4	N,N-Diethyl-	202°	3040sh,	2990sh,		*2860vs*,*	2340sh	1607vs	1540s	None
5	N-Phenyl-	182–183°	2820sh,	*2710vs*,*		2600sh,	2360m	1630vs	?	1550s
6	N-*o*-Tolyl-	214–216°	2800sh,	*2680vs*,*		2600sh,	2360m	1625vs	1555m	1575m
7	N-*m*-Tolyl-	193–195°	*2830vs*,*	*2740vs*,*		2600sh,	2360w	1635s	1550m	1585m

*Very broad strong bands.

†Bands have no sharp peaks; positions of absorption maxima represent only approximate values.

TABLE II

Positions of absorption maxima (cm^{-1}) in the infrared spectra of N-substituted trifluoroacetamidine hydrochlorides

No.	Trifluoro-acetamidine hydrochlorides	M.p. (decomp.)	$\nu(\overset{+}{\underset{}{\rangle}}\!\!\overset{+}{N}H)$		and	$\nu(=\overset{+}{N}H_2)$†		$\nu(C=\overset{+}{N})$	$\delta(=\overset{+}{N}H_2)$	$\delta(\overset{+}{\underset{}{\rangle}}\!\!\overset{+}{N}H)$
1	N-Methyl-	219–221°	3150m,	2970vs,		*2910vs*,*	2780m	1717vs	1655vw	1560vw
2	N-Ethyl-	189–191°	3130m,	*2900vs*,*		2760sh,	2360w	1707vs	1650m	1560m
3	N,N-Dimethyl-	169–171°	3000sh,	*2850vs*,*		2780sh,	2330w	1655vs	1585s	—
4	N,N-Diethyl-	133–135°	2960sh,	*2780vs*,*		2360w		1645vs	1580s	—
5	N-Phenyl-	179–180°	*2840vs*,*	2770sh,		2630sh,	2360m	1685vs	1537s	1525s

*Very broad strong bands.

†Bands have no sharp peaks; positions of absorption maxima represent only approximate values.

A broad and very strong band was shown instead, between 2600 and 3000 cm^{-1}, which possessed two to three well-defined inflections. This absorption includes, of course, the CH stretching vibrations; their separation being impossible with the low dispersion prism used. In addition a broad weak absorption band appeared near 2350 cm^{-1} in all cases.

The striking feature of all the spectra was the complete absence of the strong bands near 2000 cm^{-1} (5) and between 2600 and 2000 cm^{-1}. Furthermore the strongest absorptions occurred at higher frequencies in the corresponding amine hydrochlorides, as was firmly established from a comparison of two amidine hydrochlorides with their deuterated analogues (Table III). Since the greater the positive charge on a nitrogen atom the greater is the displacement of its NH^+ stretching vibrations towards the lower frequencies (1), this observation may definitely demonstrate that only partial positive charges are present in the amidinium cation, which does not agree with structures (V) and (VI).

The stretching $\nu(C=\overset{+}{N})$ vibrations were easily detected since they showed the strongest band between 1600 and 1700 cm^{-1}. Moreover, deuterium chloride salts of two deuterated N-alkylamidines established this assignment, since they displaced all $\delta(\overset{+}{N}H)$ absorptions. This frequency seems to be quite sensitive to small changes, because substitution of the two amino and imino hydrogens by deuterium in N-methyltrifluoro- and N-methyltrichloro-acetamidine salts reduced the absorption frequency by about 20 cm^{-1}, and formula (III) indicates that some distortion of the almost planar configuration of the molecule is likely to occur.

TABLE III*a*

Absorption maxima (cm^{-1}) in the infrared spectra of N-methyltrichloro- and N-methyltrifluoro-acetamidines and their salts

No.	Compound	ν(NH)	ν(=NH)	ν(ND)	ν(=ND)	ν(NH^+)	ν(ND^+)
1	$F_3C-C(=NH)-NHCH_3$	3515	3380				
2	$F_3C-C(=ND)-NDCH_3$			2585	2470		
3	$F_3C-C(=NH)-NH(CH_3)^+$					2910	
4	$F_3C-C(=ND)-NDCH_3^+$						2200vs*
5	$Cl_3C-C(=NH)-NHCH_3$	3480	3355				
6	$Cl_3C-C(=ND)-NDCH_3$			2570	2465		
7	$Cl_3C-C(=NH)-NHCH_3^+$					2930	
8	$Cl_3C-C(=ND)-NDCH_3^+$						2260vs

*Also 2420 (s), 2190 (s), and 2110 (s) peaks.

TABLE III*b*

Comparison of ν(NH)/ν(ND) ratios of absorption maxima (cm^{-1}) in the infrared spectra of N-methyltrichloro- and N-methyltrifluoro-acetamidines and their salts

Compound No.	$\frac{\nu(NH)}{\nu(ND)}$	$\frac{\nu(=NH)}{\nu(=ND)}$	$\frac{\nu(NH^+)}{\nu(ND^+)}$
1/2	1.36	1.37	
3/4			1.32
5/6	1.31	1.31	
7/8			1.30

There was no difficulty in the identification of the $\delta(=NH_2^+)$ modes with the N-dialkyl compounds, since only one band was present and suitable for this assignment between 1530 and 1590 cm^{-1}.

Two peaks of medium to strong intensity appeared in the spectra of the N-substituted compounds. Although no decisive conclusions could be drawn, the one existing very close to the amidine II band in the corresponding free bases was attributed to the $\delta(>NH^+)$ of the secondary amino group, and the other to the $\delta(=NH_2^+)$ frequency.

The present study suggests quite clearly that protonation is always initiated at the imino group, and the distribution of the positive charge over the two nitrogens takes place in agreement with this theory.

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THE REACTION OF NITROACETONITRILE WITH AROMATIC AMINES[1]

JOHN C. GRIVAS[2] AND ALFRED TAURINS

ABSTRACT

It has been shown by infrared spectroscopic study that the alleged N-aryl-nitroacetamidines are in fact the salts of nitroacetonitrile with aromatic amines.

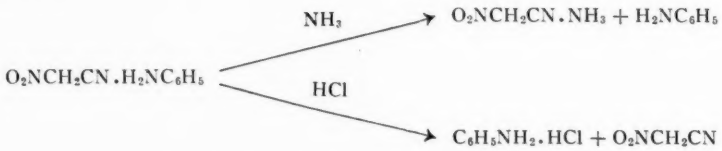
RESULTS AND DISCUSSION

Studies have been made of the reactions of nitroacetonitrile with various amines in an attempt to examine the influence of electronegative groups attached to the α-carbon atom of acetonitrile on the formation of the amidines. The reaction forming alleged N-phenyl-, N-*o*-tolyl-, and N-(2,4-dimethylphenyl)-nitroacetamidine has been reported (1) to occur almost instantaneously in ether at about 0° C.

Early observations were made, showing that ammonia gas decomposed the alleged N-phenylnitroacetamidine in ether solution, to give a precipitate of ammonium salt of nitroacetonitrile while aniline remained in solution. Passing hydrogen chloride gas through a similar solution caused the amidine to decompose into aniline hydrochloride and nitroacetonitrile.

The hydrolysis of these alleged amidines to their starting materials was attributed recently (2) to the formation of a resonance-stabilized carbonium ion, although no other amidines are known to hydrolyze in this way.

It seemed doubtful to us that the amidines of nitroacetonitrile and aromatic amines could be formed so readily, since the reaction between the more electropositive carbon atom of the carbon–nitrogen triple bond of trichloroacetonitrile, with primary aromatic amines, takes place only very slowly at room temperature, even in polar solvents (3). Furthermore, the reported behavior of the reaction products towards ammonia and hydrogen chloride, and their solubilities, could be explained better if they were salts rather than amidines. Since nitroacetonitrile is about as acidic as acetic acid, the reaction of the salts with ammonia and hydrogen chloride could then be represented by the following scheme:



In view of these contradictory facts, we have prepared the three addition compounds in question, and investigated their infrared spectra, together with that of ammonium salt of nitroacetonitrile, $NH_4^+[O_2NCHCN]^-$. The results are summarized in Table I.

The presence of very sharp strong absorption bands in the infrared spectra of the four compounds, due to the (C≡N) vibrations being very close to 2200 cm^{-1}, suggested immediately that no addition occurred across the carbon–nitrogen triple bond. The four

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Contribution from the Department of Chemistry, McGill University, Montreal, Que., with financial assistance from the National Research Council, Ottawa, Canada.
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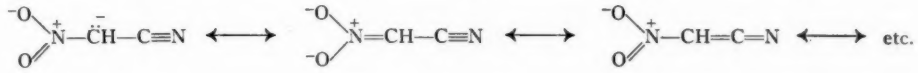
TABLE I

Positions of absorption maxima (cm^{-1}) in the infrared spectra of nitroacetonitrile salts $[O_2NCHC{\equiv}N]^-\ H_3\overset{+}{N}R$

Assignment	R = H	R = C_6H_5—	R = CH_3—OC_6H_4—	R = 2,4$(CH_3)_2C_6H_3$
$\nu(NH_3^+)$		3060m†	3100sh	3100m
		2540m	3010m‡	3000s‡
			2710m	2730s
			2560s	2580vs
			2360sh	2100m
$\nu(NH_4^+)$	3060vs*			
	2780s			
$\nu(C{\equiv}N)$	2210s	2200s	2200s	2205s
$\delta(NH_3^+)$		1578m	1535m	1623m
		1525m		
$\nu_{asym}(NO_2)$	1500vs	1480vs	1500vs	1505vs
$\delta(NH_4^+)$	1430vs			
$\nu_{sym}(NO_2)$	1345vs	1320vs	1330vs	1328vs
ν(C—N)	1185vs	1260s	1235vs	1222vs
			1222vs	1207vs
ν(C—C)	977vs	945s	955s	948vs

*Broad band at 3200–2900 cm^{-1} including Nujol absorptions.
†Broad band at 2600–3100 with inflections at 3130 and 2740 cm^{-1} including Nujol and CH absorptions.
‡Broad bands.

salts absorbed at a frequency even lower than the conjugated aliphatic nitriles (2235–2215 cm^{-1}), as one might expect for a strongly resonating carbanion structure.



On the other hand, the two NH stretching vibrations, characteristic of the N-substituted amidines, which occur between 3300 and 3500 cm^{-1} (4) were completely absent. New wide strong bands appeared in the region 2500–3100 cm^{-1}, corresponding to the (NH_3^+) modes and indicating that the aromatic amines were present in the form of salts.

Finally, resonance within the carbanion ion caused a remarkable frequency shift in the asymmetric stretching vibration of the —NO_2 group to the lower part of the absorption range (1500 cm^{-1}), whereas the similar symmetric mode showed absorption at 1320–1345 cm^{-1}.

EXPERIMENTAL

The infrared spectra of the nitroacetonitrile salts were recorded on a Perkin–Elmer Model 21 double beam spectrophotometer. Nujol mulls of the solid compounds were prepared and spread between NaCl plates. A similar cell containing Nujol was used for compensation.

The substances were prepared according to described procedures (1, 2). They were purified in small quantities by careful sublimation at low pressure and, since they were slightly explosive, at a temperature not exceeding 50°.

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KINETIC EQUATIONS FOR ENZYME REACTIONS IN THE PRESENCE OF POWERFUL INHIBITORS[1]

RICHARD M. KRUPKA AND KEITH J. LAIDLER

ABSTRACT

Steady-state equations are worked out for the case of a competitive inhibitor that is present in concentrations comparable with that of the enzyme; allowance is made for the inhibitor attached to the enzyme. Two cases are considered: in case 1 the enzyme and inhibitor form a simple addition complex, while in case 2 a molecule is split off. Methods of graphical analysis of rate data are described.

INTRODUCTION

In the development of steady-state equations for enzyme systems (1) the assumption is generally made that the enzyme concentration is much less than the concentrations of substrates, inhibitors, and activators; allowance is therefore not made for the fact that the amounts of these substances that are present in the free state are, owing to complexing with the enzyme, less than the total amounts. This assumption is justified for most systems. However, when very powerful inhibitors such as diisopropyl phosphorofluoridate (DFP) are present their molar concentrations are frequently comparable with those of the enzyme. There is, therefore, need for steady-state equations appropriate to this situation.

Such equations are developed in the present paper, and they are applied to some data obtained in the following paper. Two cases are considered: in the first, the enzyme forms a simple addition compound with the inhibitor, while in the second the complexing is accompanied by the splitting-off of a molecule. In both cases the inhibition is regarded as competitive, since this appears always to be the situation for inhibitors of this type.

STEADY-STATE EQUATIONS

Case 1: The Enzyme and Inhibitor Form a Simple Addition Complex

This case is represented by the equations

$$E+S \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} ES \xrightarrow{k_2} E+\mathrm{P}$$

$$E+I \overset{K_1}{\rightleftarrows} EI.$$

K_1 is the equilibrium constant for the formation of the enzyme–inhibitor complex, and is defined by

$$[1] \qquad K_1 = [\mathrm{EI}]/([\mathrm{E}][\mathrm{I}]).$$

A constant $\tilde{K}$, equal to the reciprocal of the conventional Michaelis–Menten constant, is defined by

$$[2] \qquad \tilde{K} = [\mathrm{ES}]/([\mathrm{E}][\mathrm{S}]) = k_1/(k_{-1}+k_2).$$

[1]*Manuscript received February 27, 1959.*
Contribution from the Department of Chemistry, the University of Ottawa, Ottawa, Canada.

Can. J. Chem. Vol. 37 (1959)

The total concentrations of enzyme and inhibitor are given by

[3] $$[E]_0 = [E]+[ES]+[EI]$$

[4] $$[I]_0 = [I]+[EI].$$

The rate in the absence of inhibitor is given by

[5] $$v_0 = (k_2\tilde{K}[E]_0[S])/(1+\tilde{K}[S])$$

while the general rate is given by

[6] $$v = k_2[ES] = k_2\tilde{K}[E][S].$$

From [5] and [6] it follows that

[7] $$[E] = \frac{v}{v_0}\frac{[E]_0}{1+\tilde{K}[S]}$$

and

[8] $$[ES] = \frac{v}{v_0}\frac{[E]_0\tilde{K}[S]}{1+\tilde{K}[S]}.$$

From [3] and [4] it follows that

[9] $$[EI] = (K_1[E][I]_0)/(1+K_1[E])$$

and using [7],

[10] $$[EI] = \frac{vK_1[E]_0[I]_0}{v_0(1+\tilde{K}[S])+vK_1[E]_0}.$$

Introduction of the expressions [7], [8], and [10] into eq. [3] gives rise to

[11] $$[E]_0 = \frac{v}{v_0}[E]_0+\frac{vK_1[E]_0[I]_0}{v_0(1+\tilde{K}[S])+vK_1[E]_0}.$$

This rearranges to

[12] $$[I]_0+\left(\frac{v}{v_0}-1\right)[E]_0 = \left(\frac{v_0}{v}-1\right)\frac{1+\tilde{K}[S]}{K_1}.$$

Experimental results for this type of system may therefore be analyzed by plotting

$$[I]_0+\left(\frac{v}{v_0}-1\right)[E]_0$$

against $(v_0/v-1)$ for a given substrate concentration; from the slope of the line K_1 can then be calculated provided that $\tilde{K}$ is known from separate studies in the absence of inhibitor. An example of this type of plot is shown below.

Case 2: Complexing Associated with the Splitting-off of a Molecule

This case is represented by

$$E+S \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} ES \xrightarrow{k_2} E+P$$

$$E+I \overset{K_1}{\rightleftarrows} X+Y$$

where X is the complex and Y the molecule split off. The concentrations of X and Y must always be identical, and will be written as [X].

Equations [1] to [4] are now replaced by

[13] $$K_1 = [X]^2/([E][I])$$

[14] $$\bar{K} = [ES]/([E][S])$$

[15] $$[E]_0 = [E]+[ES]+[X]$$

[16] $$[I]_0 = [I]+[X].$$

From [13] and [16] it follows that

[17] $$[X]^2+K_1[E][X]-K_1[E][I]_0 = 0.$$

From [7] and [8]

[18] $$[E]+[ES] = (v/v_0)[E]_0$$

so that using [15]

[19] $$[X] = [E]_0\left(1-\frac{v}{v_0}\right).$$

Introduction of [7] and [19] into [17] gives

[20] $$[E]_0^2\left(1-\frac{v}{v_0}\right)^2+K_1\frac{v}{v_0}\frac{[E]_0^2}{1+\bar{K}[S]}\left(1-\frac{v}{v_0}\right)-K_1\frac{v}{v_0}\frac{[E]_0[I]_0}{1+\bar{K}[S]} = 0,$$

which reduces to

[21] $$1-\frac{v}{v_0} = \frac{K_1}{1+\bar{K}[S]}\left[\frac{[I]_0}{[E]_0\{(v_0/v)-1\}}-\frac{v}{v_0}\right].$$

The value of K_1 could now be determined from a plot of $1-v/v_0$ against

$$\frac{[I]_0}{[E]_0\{(v_0/v)-1\}}-\frac{v}{v_0}.$$

APPLICATION TO EXPERIMENTAL DATA

In the work described in the following paper rates have been measured for the α-chymotrypsin-catalyzed hydrolysis of hydrocinnamic ester, over a range of pH values and of concentrations of DFP. Figure 1 shows a case 1 plot for the rates obtained at pH 8.1; the experimental details are given in the following paper. The plot is seen to be satisfactorily linear when the degree of inhibition $(v_0/v-1)$ is small. At high inhibitor concentrations, however, there are very significant deviations from linearity, in the sense that the inhibition is much greater than would be predicted from the behavior at low inhibitor concentrations. This effect is attributed tentatively to the formation of a second complex of the type EI_2, as found with other enzyme–substrate systems (for example, urease (2), carboxypeptidase (3), acetylcholinesterase (4); cf. also ref. 1, pp. 71–77, 260–263).

The slope of the linear portion of the curve is 1.93×10^{-6}, and from this, since $[S] = 1.17\times10^{-3}$ and $\bar{K} = 2500$, a value of 2.04×10^6 is calculated for K_1. It is of interest that use of the simple conventional inhibition equation

[22] $$v/v_0 = (1+\bar{K}[S])/(1+\bar{K}[S]+K_1[I])$$

leads to a K_I value of 1.2×10^6, which is much less than the true value. The equations developed in the present paper will always give higher K_I values than the simple formula, which overestimates the concentrations of inhibitor present free in the solution.

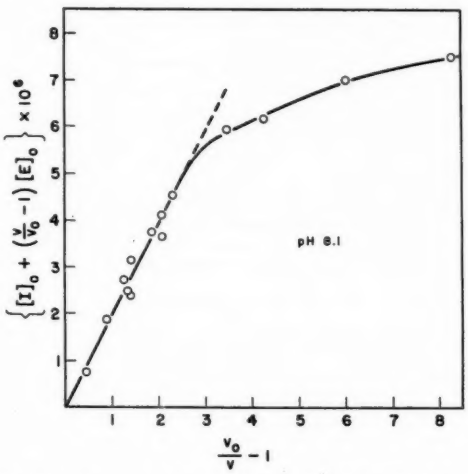

FIG. 1. A plot showing that the mechanism of case 1 is applicable at low inhibitor concentrations.

A plot of the data according to the case 2 mechanism did not give a straight line even at low inhibitor concentrations, and it is concluded that this situation is not applicable. Although the reaction of DFP with the enzyme is accompanied by the liberation of HF (5), it may be that the fluoride ions remain attached to the protein so that equation [1] applies rather than equation [13].

ACKNOWLEDGMENT

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KINETICS OF THE INHIBITION OF α-CHYMOTRYPSIN BY METHANOL AND DFP[1]

BERNARD R. STEIN[2] AND KEITH J. LAIDLER

ABSTRACT

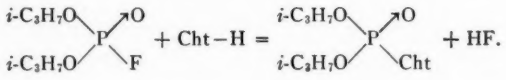
A study has been made of the kinetics of the α-chymotrypsin-catalyzed hydrolysis of methyl hydrocinnamate in the presence of various concentrations of methanol, of eserine, and of diisopropyl phosphorofluoridate (DFP). In 20% methanol the pH optimum, using a substrate concentration of 1.20×10^{-3} *M*, is 7.8; in pure water it is 8.3; and at intermediate pH's the optimum varies between these values. No inhibition was observed with eserine. In aqueous solution the character of the inhibition by DFP differs from that in alcohol solutions; the inhibition is of the competitive type, and the inhibition constant varies with pH in essentially the same manner as does the rate of the reaction. This result suggests that DFP interacts with the same active groups on the enzyme as are responsible for the hydrolysis of the substrate. A specific mechanism for inhibition is suggested.

INTRODUCTION

Studies of the influence of inhibitors on the rates of enzyme reactions have contributed considerably to an understanding of the mechanisms of enzyme action. In a recent paper (1) the kinetics of the α-chymotrypsin-catalyzed hydrolysis of methyl hydrocinnamate have been studied in the presence of hydrocinnamic acid, and it has been concluded that this inhibitor interacts with the enzyme at its active center, and that this active center contains a negatively charged group in addition to the acidic and basic groups actually responsible for the hydrolysis of the substrate.

In the present investigation this general line of attack on the chymotrypsin system has been extended to a study of the inhibition of the enzyme by methanol and by diisopropyl phosphorofluoridate (DFP). The main purpose of the work with methanol was to relate previous kinetic studies in 20% methanol–water mixtures with those that we are at present carrying out in pure aqueous solutions. Since 20% methanol solutions are far from physiological, and since (as shown below in the case of inhibition by DFP) the behavior is sometimes quite different in the two media, it seemed to be of interest to carry out kinetic studies in pure water and to relate the results to those obtained in the presence of alcohol.

The inhibition of α-chymotrypsin by DFP has been very thoroughly investigated (2, 3, 4, 5, 6, 7, 8, 9) but always, it would appear, using solvents containing propanol or other alcohols. Under the conditions previously employed the DFP reacts stoichiometrically with the enzyme, with the release of hydrogen fluoride, in accordance with the following equation:



In previous studies this reaction has appeared to proceed essentially to completion, although the inhibitor can be displaced from the enzyme by the action of electrophilic reagents such as hydroxylamine (10, 11, 12, 13, 14, 15, 16).

In our experiments in pure aqueous solutions we have found definite evidence for reversibility; the DFP indeed acts as a competitive inhibitor. The behavior has been

[1]*Manuscript received February 27, 1959.*
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investigated over a range of inhibitor concentrations and pH values, and conclusions drawn about the nature of the interaction between the DFP molecule and the active center of the enzyme.

EXPERIMENTAL

Materials

The enzyme and ester were as described in the previous paper (1), and the methanol was purified by distillation. The DFP was a pure sample supplied by the Defence Research Chemical Laboratories, Shirley Bay, Ontario.

Kinetic Procedure

The rate measurements were carried out using a pH-stat, manufactured by the Ole Dich Company of Copenhagen, together with a radiometer automatic titrator. Calomel and glass electrodes in the reaction mixture together with the titrator allowed the pH to be recorded, and when the pH fell below the designated value the pH-stat injected 0.02 *M* sodium hydroxide from a syringe micropipette into the reaction system. The pH-stat contains a rotating drum on which a record is made of alkali added vs. time; since the alkali is added in increments of about 10^{-4} cc, the record is extremely smooth and allows rates to be measured with great accuracy. All rates quoted are initial rates.

The reaction vessel was a small glass cell maintained at constant temperature (20.0° C) by circulation of thermostatically controlled water through an outer jacket. Fifteen milliliters of reaction mixture was employed in each case, and stirring was done magnetically. Various enzyme concentrations were employed, mostly in the region of 3×10^{-6} *M*. Owing to the limited solubility of the substrate in pure water, runs could not be done at concentrations higher than about 3×10^{-3} *M*; most were done at about 1.2×10^{-3} *M*. To avoid changes in ionic strength all runs were carried out at a sodium chloride concentration of 0.1 *M*. The total volume of sodium hydroxide solution added during a run never exceeded 3% of the total volume, and was usually less than this; the correction required is therefore very small.

RESULTS

Inhibition by Methanol

The work of Laidler and Barnard (17) showed that in 20% methanol there is a well-defined pH optimum at 7.8. In the present study runs were made at methanol concentrations varying from zero to 12%, and at pH values ranging from 7.5 to 8.5. The results are shown in Table I and Fig. 1, in which are included the rates measured by Laidler and Barnard (17) in 20% methanol–water mixtures.

TABLE I

Rate of hydrolysis of hydrocinnamic ester in the presence of methanol
Rates in $mole^{-1}\ sec^{-1}\times10^{9}$ Temperature = 20.0° C
$[E]_0 = 3.33\times10^{-6}$ *M* [S] = 1.2×10^{-3} *M* [NaCl] = 0.1 *M*

% Methanol (by volume)	Rate at pH				
	7.5	7.8	8.1	8.3	8.5
0	138.7	160.3	185.5	190.7	165.2
0.66	100.8	136.1	150.0	151.7	133.2
2.0	70.8	91.2	100.0	96.5	82.7
4.0	39.4	59.1	68.0	63.0	56.7
8.0	18.5	29.0	31.4	28.0	23.4
12.0	12.5	21.0	21.9	18.0	11.2
20.0	5.0	8.5	7.5	5.5	3.0

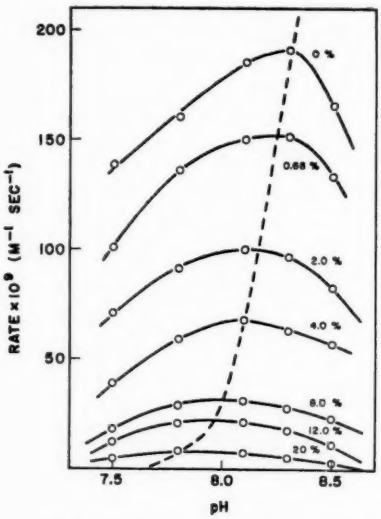
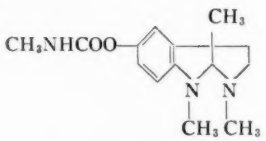


FIG. 1. Plots of rate against pH for various concentrations of methanol. The dotted line shows the variation of the pH optimum.

Lack of Inhibition by Eserine

Since eserine (physostygmine), which has the structure



is a very powerful inhibitor for cholinesterase, a study has been made of its action on chymotrypsin. Rate measurements have been made, using the same conditions as above, at pH values varying from 7.5 to 8.7 and at eserine:enzyme molar ratios of up to 40. There was no inhibition under any of the conditions employed.

Inhibition by DFP

In the majority of our experiments with DFP the procedure was to add the aqueous solution of the inhibitor to the enzyme solution which had previously been brought to the required pH by addition of sodium hydroxide; this addition was carried out slowly with the vessel connected to the pH-stat, so that no change in pH occurred, and the mixture was then allowed to stand, with stirring, for 10 minutes. The substrate was then added slowly and the reaction followed with the recorder.

Table II shows some typical results using this procedure. It is to be noted that even when the inhibitor was considerably in excess of the enzyme the inhibition is not complete; this was the case even when the inhibitor–enzyme ratio was as high as 4:1. This result is in marked contrast to that obtained by Jansen and co-workers (2), who used a propanol–water mixture as solvent and acetyl tyrosine ethyl ester as substrate. They found that when the molar ratio of DFP to enzyme was greater than unity there was

TABLE II

Typical results showing that the DFP inhibition is reversible
Temperature = 20.0° C
[NaCl] = 0.1 M [S] = 1.17×10^{-3} M $[E]_0 = 3.03\times10^{-6}$ M

[DFP] $\times10^6$	$[DFP]/[E]_0$	% inhibition
1.18	.39	17.0
2.36	.78	28.6
3.54	1.17	45.1
4.72	1.56	48.0
5.36	1.77	61.8
8.04	2.65	83.2
10.72	3.54	87.8

practically 100% inhibition. This observation was confirmed by us using their experimental conditions, but using pure water as solvent the inhibition was much less strong, as shown in Table II. We tentatively attribute this difference to the fact that the alcohol interacts with the HF formed and in this way displaces the equilibrium.

The interaction between DFP and chymotrypsin is thus reversible under our conditions. Experiments were also carried out to determine whether the behavior was competitive or non-competitive with respect to the substrate. This was done by determining the degree of inhibition at various substrate concentrations; the degree of inhibition was found to be reduced by increasing the substrate concentration, so that it is concluded that the behavior is competitive.

The above work was done by measuring initial rates. Further evidence that the inhibition is reversible and competitive under our reaction conditions was provided by studies of the time course of the reactions. Experiments were carried out in which the DFP and substrate were mixed first, after which the enzyme was added. It was found that the greater the substrate: inhibitor ratio the less was the falling-off of the rate as the reaction proceeded. It follows that the substrate competes with the inhibitor and can displace it from the enzyme surface.

Measurements were then carried out with a view to determining the association constant K_1 between the enzyme and the inhibitor. In this series of experiments the enzyme and inhibitor were mixed first, after which substrate was added and initial rates measured using the pH-stat.

As discussed in the preceding paper, the inhibition by DFP can, at low inhibitor concentrations, be interpreted in terms of the mechanism

$$E+S \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} ES \xrightarrow{k_2} E+P$$

$$E+I \overset{K_1}{\rightleftarrows} EI.$$

Allowance must be made for the inhibitor that becomes bound to the enzyme, and the resulting kinetic equation is [12] of the preceding paper.

The data have been analyzed in terms of this equation, and plots similar to that of the preceding paper were obtained at all pH values. The resulting K_1 values are shown in Table III. The variation of K_1 with pH is shown in Fig. 2, which also shows the variation of rate with pH at a substrate concentration of 1.20×10^{-3} M.

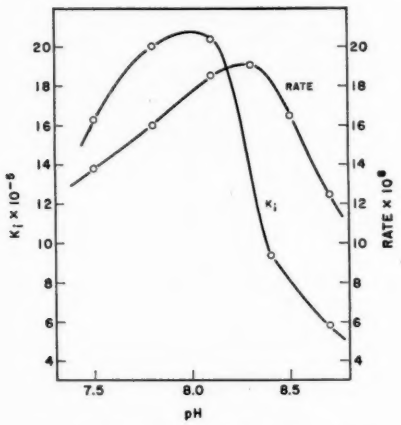


FIG. 2. Plots of K_i against pH and of rate against pH at a substrate concentration of 1.20×10^{-3} M.

TABLE III

Results for the inhibition of α-chymotrypsin by DFP

Temperature = 20.0° C

[NaCl] = 0.10 M [S] = 1.17×10^{-3} M $[E]_0 = 3.03\times10^{-6}$ M

pH	$\bar{K}$	$(1+\bar{K}[S])\times10^6/K_i$	$K_i\times10^{-5}$
7.5	2730	29.6	14.2
7.8	2600	2.03	19.9
8.1	2500	1.93	20.4
8.4	2010	3.58	9.35
8.7	1570	4.96	5.72

DISCUSSION

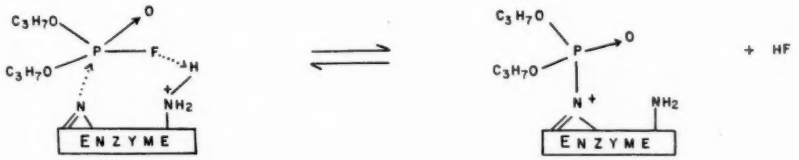
The influence of methanol on the kinetics of the α-chymotrypsin – hydrocinnamic ester system was treated by Barnard and Laidler (18) as a dielectric constant effect. This may well be the case under the conditions of the previous experiments, in which the methanol concentration varied from 15 to 25%. However, the very marked inhibition brought about by small amounts of methanol, as found in the present work, is too great to be explained as a solvent effect, and is probably due to a specific interaction between the enzyme and the methanol. The methanol may well interfere with hydrogen bonding at the active center and in this way affect markedly the interaction between the enzyme and the substrate. The small shift in pH optimum is understandable on the same basis.

The complete lack of inhibition by eserine indicates that the negatively charged group on the chymotrypsin molecule (indicated by the work with hydrocinnamic acid (1)) is not able to interact with a positively charged group on the eserine molecule. This anionic site on chymotrypsin therefore differs in character from that on the cholinesterase molecule, which is markedly inhibited by eserine.

The most significant result of the present investigation is that the inhibitor constant K_i varies with pH in approximately the same manner as does the reaction rate itself. It follows from this that the reaction between the enzyme and DFP is of a similar nature to that between the enzyme and the substrate.

Previous work, including studies of the pH dependence of the rate (17, 19, 20, 21),

has suggested that the hydrolytic action of the enzyme involves a simultaneous nucleophilic attack by an imidazole nitrogen atom and an electrophilic attack by a protonated ω-amino ion. It is postulated that a similar process occurs when the enzyme forms a complex with the DFP molecule, and the reaction may be represented as



This proposal relates to the reversible binding of the inhibitor. The irreversible inhibition may be due to the transfer of the $(C_3H_7O)_2PO$- group from the imidazole ring to a neighboring serine residue.

ACKNOWLEDGMENTS

The authors are indebted to Mr. E. K. Gill for help with the experimental work and to Dr. R. M. Krupka for help with the analysis of the experimental data. They are also grateful to the Defence Research Board for their support of this work under Grant DRB 9510-06.

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NOTE ON THE DETECTION OF AN APPARENT PHASE TRANSITION OF ADSORBED WATER ON POROUS VYCOR GLASS BY MEASUREMENTS OF DIMENSIONAL CHANGES[1]

C. HODGSON[2] AND R. MCINTOSH

ABSTRACT

A new technique is described for detecting possible phase transitions of adsorbates. The method involves the measurement of length changes of the solid, but only solids for which the surface-to-volume ratio is large could be used with the present form of instrument because of its moderate sensitivity. Using this measurement an apparent phase transition for water adsorbed on porous Vycor glass has been detected at approximately −22° C.

The detection of phase changes occurring in adsorbates on solids has been attempted in a variety of ways. Among these are the dependence of equilibrium pressure on temperature, the anomalies of carefully determined cooling curves, and dilatometric techniques (1, 2, 3). The experimental evidence is not always readily acceptable because of the methods employed.

Recently Puri, Singh, and Myer (4) reported the experimental detection of the formation of the "solid" phase for a variety of adsorbate–adsorbent systems by means of measurements of equilibrium pressures. These authors compared their data with predicted freezing point depressions based upon the Kelvin theory of capillary condensation and the assumption that the adsorbed "solid" would have the same equilibrium vapor pressure as that of bulk solid. This implies that the adsorbed "solid" is not under any negative pressure due to concave menisci, which could well be valid, and also that the adsorbed "solid" has the properties of bulk solid, which is unlikely. The validity of the latter assumption could be directly established by a measurement of equilibrium pressure over the adsorbate.

In view of the earlier work from this laboratory (5, 6), the contraction of the adsorbent system due to concave menisci seems reasonably well established. If the effects of menisci could be appreciably changed by forming the solid phase a marked expansion of the system might be expected. It should be noted that the change of molar volume of the adsorbate could also produce an effect. Discrimination between these two causes should be possible using an adsorbate for which the solid molar volume is less than that for liquid, e.g. benzene. A further reason to employ such an adsorbate is given below.

An expansion on lowering temperature, and a contraction through the same range of temperature when the system is rewarmed, have now been established for water adsorbed on porous Vycor glass (see Fig. 1). The phenomenon may exist for water contents below the beginning of the hysteresis loop, but experimental precision in determining length changes makes this speculation. However, because the extent of the anomaly increases markedly for water contents above the inception of the hysteresis loop the effect is probably associated with water condensed in the pores.

The Kelvin theory as applied by Puri, Singh, and Myer (4) does not rationalize our experimental observations since (*a*) the transition should be sharp as all the liquid menisci have the same radius of curvature for a given relative pressure, and (*b*) the transition temperature should depend upon the relative pressure corresponding to the adsorbate content.

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Contribution from the Department of Chemistry, University of Toronto, Toronto, Ontario.
[2]*Graduate Student and holder of N.R.C. Studentship (1958–59), Union Carbide Fellowship (1957–58).*

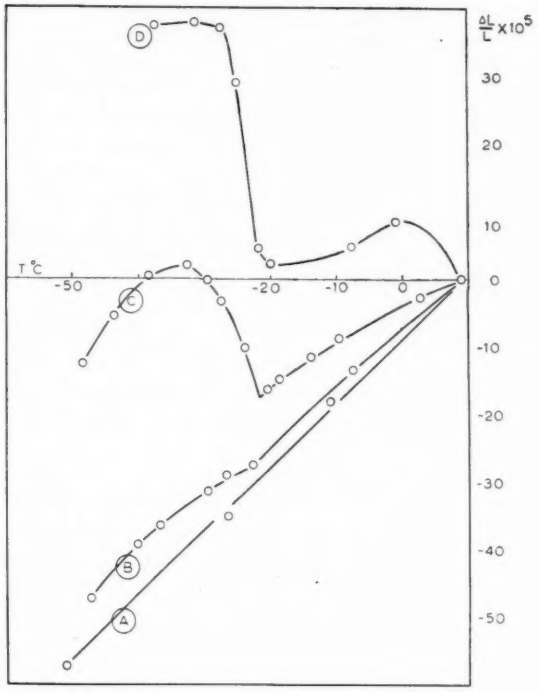

FIG. 1. Plot of fractional length change against decreasing temperature for water contents of:
A, 0.0221 g per g. C, 0.175 g per g.
B, 0.138 g per g. D, 0.195 g per g (desorption branch).

Curve "A" in Fig. 1 for a water content of 0.0221 g water per g glass, i.e. well below the beginning of the hysteresis loop, is approximately linear; curve "B" for a water content on the lower part of the adsorption branch of the hysteresis loop begins to show a slight anomaly at −22° C; while curves "C" and "D" show large anomalies. In the cases "C" and "D" the water contents are high on the adsorption and desorption branches respectively, but the evidence of transition again appears at −22° C in both cases. An unexplained hysteresis on reversing the direction of temperature change has been observed, but has been omitted from the figure.

For a given quantity adsorbed, the transition temperature of the adsorbed matter, relative to that of bulk material, depends upon the relative displacements of the molar free energy versus temperature curves of the adsorbed phases from those of the bulk. The assumption of concave menisci for the adsorbed "liquid" predicts a lowering of its curve relative to that for bulk liquid. The same assumption might be made in dealing with the "solid" phase except for the difficulty of obtaining the value of the surface free energy of the "solid". As pointed out above, the molar free energy of the adsorbed "solid" would be expected to be lower than that of the bulk solid but we have been unable to determine the low pressures with sufficient accuracy to establish the relative values. However, the known compressibility of Vycor-adsorbate systems (7), the negative pressure generated by the liquid menisci, and the measured expansion of about 20 μ in

the transition range (see system "C") combine to suggest that the effect of concave menisci has not been completely eliminated after the transition to "solid".

Whether or not effects due to menisci must be assumed for the "solid" adsorbate can be demonstrated. Hysteresis is caused, in the general view, by the shapes of the voids and the radius of curvature of menisci appropriate to the adsorption or desorption conditions. Thus hysteresis should vanish from an isotherm determined at a temperature where "solid" adsorbate is the stable form, provided that effects due to menisci do not exist for the "solid" phase. The equilibrium pressures for water are too low to make this test conveniently, but it might be possible using benzene. The necessary experiments are now being begun.

Full details of the experiments with water and an expanded discussion of the thermodynamic theory will be published at a later date.

The authors would like to express their thanks to Dr. M. H. Panckhurst for many helpful discussions. Grateful acknowledgment is also made to the National Research Council and to the Advisory Committee on Research, University of Toronto, for financial support of this work.

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ULTRAVIOLET IRRADIATION OF PYRIMIDINE DERIVATIVES

III. INFLUENCE OF HYDROGEN CYANIDE ON THE PHOTOLYSIS[1]

A. M. Moore

ABSTRACT

The presence of HCN in concentrations up to 0.05 *M* in aqueous, buffered solutions of uracil, uridine, and 1,3-dimethyluracil has been shown to divert the normal course of the photochemical hydration reactions of these compounds as a result of photochemically induced combination between HCN and the pyrimidine derivative. A simple calculation indicates that HCN is more efficient than water in reacting with activated uracil molecules by a factor of about 10^3. The possible general significance of such nucleophilic addition reactions in the photochemistry of nucleic acids is discussed.

INTRODUCTION

Evidence has been accumulating during the past 5 years (reviewed in 11) to indicate that the principal initial photochemical reaction of aqueous solutions of uracil and cytosine, their nucleosides, and nucleotides consists of the addition of a molecule of water to the 5,6 double bond of the pyrimidine ring. The studies that have been reported in this connection have been made with dilute solutions of the pyrimidine compounds in water or in buffer. Although it is interesting to speculate from such evidence about the possible biological significance of the photochemical hydration reaction, it is important to remember that our knowledge of such reactions is very limited and that, in any case, the analogy between the simple aqueous systems that have been studied and the situation involved in the irradiation of complex nucleic acid molecules in vivo leaves something to be desired.

The present paper reports the results of a study of the influence of hydrogen cyanide, in low concentration, upon the course of the photochemical hydration of uracil and certain of its derivatives. The rather large effect observed makes it clear that the course of the hydration reaction may be greatly modified by the presence of other components of the solution.

The choice of hydrogen cyanide for these experiments was, of course, made not on physiological but on chemical grounds. The addition of hydrogen cyanide and other weak acids to conjugated mono-olefinic carbonyl compounds—in which class we may include uracil and its derivatives—has been extensively studied (cf. for example, ref. 3). Furthermore, the ready availability of carbon-14-labelled cyanide makes it a convenient tool for such study.

METHODS

General

Irradiations were carried out with the apparatus previously described (8) using low-pressure mercury arcs (wavelength mainly 2537 Å) as light source. The spectroscopic changes were determined on samples withdrawn after various irradiation times with either a Beckman DU or DK2 spectrophotometer.

The solutions which were irradiated contained the pyrimidine compounds (10^{-4} *M*), phosphate buffer (0.5 *M*, pH 7.0), various concentrations of HCN added from a stock solution of KCN (0.5 *M*) which was titrated to pH 7.0 with HCl just before use, and KCl,

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Contribution from the Biology Branch, Atomic Energy of Canada Limited, Chalk River, Ontario.
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added as required, so that all solutions had the same total chloride concentration (0.05 *N*).

The uracil and uridine used in these experiments were obtained commercially. The former was recrystallized twice from water and dried at room temperature *in vacuo*. The 1,3-dimethyluracil was prepared from this purified uracil by the method of Davidson and Baudisch (2) and was purified by recrystallization from 95% ethanol, (m.p. 122° C; $\epsilon = 8600$ at 2660 Å). The KCN and KCl were reagent grade.

C^{14}-Labelled Compounds

The $HC^{14}N$ was prepared by the method of McCarter (4) starting with $BaC^{14}O_3$ provided by Atomic Energy of Canada Ltd. As the final stage of purification it was distilled into 0.1 *N* KOH in which form it was stored until required.

The uracil-2-C^{14} was the same preparation as that previously reported (6).

EXPERIMENTAL AND RESULTS

Effect of HCN *on the Irradiation of Uracil*

Solutions of uracil were irradiated in the presence of HCN in concentrations ranging from zero to 0.05 *M*. The results (Fig. 1) show that the presence of HCN accelerated the photochemical destruction of uracil in a striking manner. Unirradiated controls showed no change in spectrum on standing in the presence of 0.05 *M* HCN for periods up to 30 minutes.

It has been reported (13) that, without HCN, about 50% of the uracil destroyed by irradiation with filtered 2537 Å light may be regenerated by heating or by acid treatment. In our own experiments, using the unfiltered light from low-pressure mercury arcs, 42–43% of the loss in optical density (2600 Å) produced by irradiation was restored by heating (100° C; 5 minutes; pH 1), and this proportion was independent of the extent of decomposition for optical density decreases of 51 to 86%. On the other hand, after irradiation (6 minutes) in the presence of 0.05 *M* HCN until the optical density had decreased by 67%, the restoration on heating amounted to only 6.5%.

Effect of HCN *on the Irradiation of 1,3-Dimethyluracil*

The quantum yield for the photodecomposition of 1,3-dimethyluracil in simple aqueous solution is about twice as large as that for uracil (see 11), and the photodecomposition curves are correspondingly steeper. No effect of HCN on the rate of reaction was observed. However, after irradiation until the optical density had fallen to 8–9% of its initial value, it was found that the extent of recovery that ensued upon heating decreased as the concentration of HCN was increased. Thus, for HCN concentrations of 0, 0.005, 0.01, and 0.05 *M* the recoveries were 100, 93, 91, and 70% respectively. Without irradiation no effect of HCN (0.05 *M*) on the spectrum of 1,3-dimethyluracil was detectable.

Effect of HCN *on the Irradiation of Uridine*

Uridine, like uracil, was decomposed more rapidly in the presence of HCN (0.05 *M*) than in simple aqueous solution (Fig. 2). A sample which had been irradiated for 5 minutes in the presence of 0.05 *M* HCN was subsequently heated to promote regeneration of the uridine. The spectrum, after this treatment, indicated that partial recovery had occurred. The final optical density at 2610 Å was only about 38.9% of the density before irradiation. By contrast, uridine irradiated in the absence of cyanide gave 97.5% recovery on heating. This latter finding agrees with the observation of Rapport and Canzanelli (10) of virtually 100% regeneration of uridine after irradiation in water for short times.

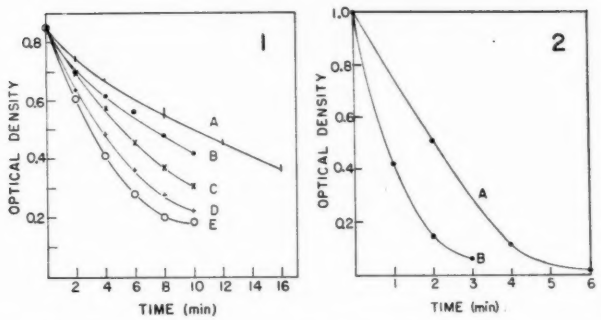


FIG. 1. Irradiation of uracil (10^{-4} *M*) in presence of various concentrations of HCN. All solutions, pH 7.0.

Curve	A	B	C	D	E
Concentration of HCN	0	0.01 *M*	0.02 *M*	0.03 *M*	0.05 *M*

FIG. 2. Irradiation of uridine (10^{-4} *M*) without HCN (curve A) and with 0.05 *M* HCN (curve B).

Test for Spontaneous Reaction of Uridine with HCN

A solution 10^{-2} *M* with respect to uridine and 0.05 *M* with respect to HCN (pH 7) was allowed to stand at room temperature in a glass-stoppered flask. Samples were withdrawn at 0, 6, and 24 hours, diluted 1:100 with water, and their spectra determined. After 24 hours at room temperature a final sample was heated at 70° C for 20 minutes before dilution and examination. The absorption spectrum showed no significant change in any of these samples.

Irradiation of Uracil and Uridine in Presence of $HC^{14}N$

Although an effect of HCN on the course of irradiation was evident in the foregoing experiments, it was not certain that it involved actual combination between cyanide and pyrimidine. In order to settle this point three experiments were performed with labelled reagents. In one, uracil-2-C^{14} was irradiated along with ordinary cyanide; in the second, ordinary uracil was irradiated along with $HC^{14}N$; in the third, ordinary uridine was irradiated with $HC^{14}N$. The products of all three experiments were chromatographed together on paper using *n*-propanol: water, 70:30 by volume, as solvent, and the materials on the chromatogram were located both by autoradiography and by contact printing with ultraviolet (2537 Å) light (5) (Fig. 3).

In the experiments with labelled uracil and ordinary cyanide, three radioactive spots (R_f 0.24, 0.50, and 0.62) were found in addition to uracil itself (R_f 0.58). Ordinary uracil and labelled cyanide gave four prominent radioactive spots. Three of these (R_f 0.24, 0.50, and 0.62) evidently corresponded to the same products as were obtained with labelled uracil. The other spot (R_f 0.36) was presumably due to a substance derived only from the $HC^{14}N$ since it was absent when the labelling was reversed.

The result of the experiments with uridine tends to support this conclusion. Here again there were four main radioactive spots. One spot corresponded in position to the R_f 0.36 component of the uracil–$HC^{14}N$ lane; the other three spots (R_f 0.19, 0.49, and 0.59) appear to be the analogues of the spots at R_f 0.24, 0.50, and 0.62 observed with uracil, the slightly lower R_f values corresponding to the fact that uridine itself has a slightly lower R_f than uracil, 0.51 compared with 0.58 in this experiment.

The individual lanes of these chromatograms were also counted in a gas flow proportional counter designed for counting chromatograms. Typical results are given in Fig. 4. The two components with R_f 0.24 and 0.62, respectively, in the uracil–HCN lanes were

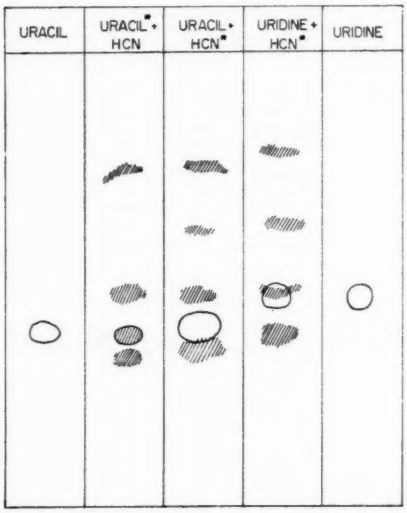


FIG. 3. Paper chromatogram of products of irradiation of pyrimidines in presence of HCN. C^{14}-Labelled reagents are indicated by asterisks in the column headings. Ultraviolet-(2537 Å)-absorbing spots are outlined; radioactive spots, located by autoradiography, are indicated by diagonal shading.

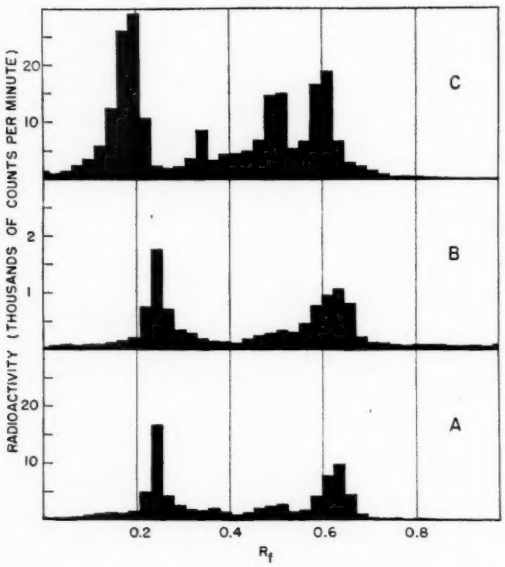


FIG. 4. Reaction products formed on irradiating pyrimidines (0.01 *M*) with HCN (0.05 *M*). 50-μl samples were chromatographed on paper (*n*-propanol: water 70:30 v/v) and the lanes were counted separately with a gas flow proportional counter. (A) Ordinary uracil and labelled HCN irradiated 6 hours. (B) Labelled uracil and ordinary HCN irradiated 4 hours. (C) Uridine and labelled HCN irradiated 3 hours.

approximately equal in amount and together accounted for 80 to 90% of the activity on the lanes in different runs, while the component with R_f 0.50 accounted for about 10% of the activity. In the uridine–HCN experiments the component of R_f 0.19 amounted to about 42% of the total activity and those with R_f 0.49 and 0.59 each contributed about 25% of the total activity.

The products of the uracil–HCN experiments were also chromatographed using *n*-butanol saturated with water as developing solvent. Irrespective of which component carried the C^{14} initially, the chromatograms exhibited three prominent radioactive components of R_f 0, 0.27, and 0.37. An additional minor component of R_f 0.11 was present in the experiments in which the HCN was labelled.

DISCUSSION

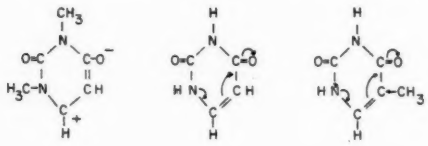
The experiments described in the foregoing pages show that when HCN is present during the irradiation of uracil, 1,3-dimethyluracil, or uridine, the activated pyrimidine reacts preferentially with it. This is made clearly evident by the extent to which the presence of the HCN reduces the yield of "reversible" product in all three cases, by the net increase in the rate of photochemical destruction of uracil and uridine, and by the chromatographic analysis of the products of irradiation using C^{14}-labelled reagents. It was also shown that the reactions with HCN were photochemical, not spontaneous.

The fact that 0.05 *M* HCN largely suppresses the formation of the "reversible" product in the case of uracil suggests that HCN is particularly efficient in competing with water for the excited uracil molecules. This matter is considered in detail in the appendix to this paper in which it is estimated that the specific reaction rate of excited uracil molecules with HCN is greater than that with water by a factor of about 10^3.

The chromatographic experiments using C^{14} demonstrated that there were multiple products. Uracil and uridine each yielded three principal products of reaction with HCN, which account for about 90% of the total reaction in each case. The most likely product in the reaction with uridine would be the nitrile of 5,6-dihydroorotidine. Other possibilities include the isonitrile and its hydrolysis products. At present the evidence does not permit a decision regarding the identity of the observed products but it may be noted that the disappearance of the ultraviolet absorption maximum (ca. 2600 Å) suggests reactions that eliminate the 5,6 double bond of the pyrimidine ring.

These results with cyanide fit into a general scheme according to which nucleophilic addition may be considered the primary photochemical reaction of the uracil derivatives. Mulliken (9) and Braude (1) have developed the concept that the first electronic excited state of compounds such as the aromatic ketones may be represented as a zwitterion with the negative charge on the oxygen and the positive charge on a carbon at the opposite end of the conjugated chain. Wang (14) has applied this concept to the pyrimidines, suggesting that the absorption of an ultraviolet quantum by a molecule of 1,3-dimethyluracil, in water solution, converts it to the structure I, which then undergoes a typical nucleophilic addition reaction with water.

The original state of polarization of the pyrimidine ring would be expected to have a considerable effect on the probability of attaining such a structure. For example, comparing uracil (II) with thymine (III) the hyperconjugating effect of the methyl group at position 5 would be expected to oppose the development of a positive charge on the carbon at position 6 thereby making thymine less susceptible than uracil to nucleophilic addition at the 5,6 double bond. In fact, thymine is much more resistant than uracil to photodecomposition and does not appear to undergo the 5,6 hydration reaction (12).



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Extending the concept one would predict that other nucleophilic agents might be induced to participate in the photochemical reactions of the pyrimidines. The results of the present experiments support this prediction. Observations have also been reported (7, 11) to indicate that ethanol, like water, undergoes reversible addition to the 5,6 double bond of 1,3-dimethyluracil and uracil under the influence of ultraviolet light.

There is thus a growing body of evidence supporting the view that photoinduced nucleophilic addition may be a general reaction of the substituted uracils. Not all additions of this sort will be as easily reversed as in the case of water; indeed the addition of cyanide appears to be irreversible. In considering the fate of pyrimidines irradiated in vivo we may expect to encounter other examples of a similar nature. Such reactions might be significant when pyrimidines are irradiated as constituents of nucleic acid molecules, where they are ideally situated to undergo reactions with neighboring pyrimidines or purines especially in structures like the Watson–Crick model of deoxyribonucleic acid (15).

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APPENDIX

The absorption of ultraviolet light by a uracil molecule raises it into an excited state. Its excitation energy may then be dissipated by both physical and chemical processes. The principal physical process is likely to be the transfer of vibrational energy to the solvent water molecules during collisions. Fluorescence has not been observed and is, in any case, unlikely because the lifetime of excited molecules with respect to radiation is generally long compared with the interval between collisions with the solvent molecules. The chemical processes, on the other hand, are known to be of two kinds: one

leading to a labile product that is capable of regenerating uracil, and another (or possibly more than one) leading to irreversible destruction of uracil. These two processes have roughly equal quantum yields (13).

The net effect of the physical and chemical processes of energy dissipation together with a fixed rate of energy input will be the establishment of an equilibrium concentration of excited molecules $[u^*]$ which will vary with time during irradiation. It will be convenient to refer to its initial value as $[u^*]_0$.

We may thus summarize the processes of energy dissipation:

[1] $$u^* + H_2O \xrightarrow{k_1} u.HOH \text{ (reversible chemical reaction)},$$

[2] $$u^* \xrightarrow{k_2} X \text{ (irreversible chemical reaction)},$$

[3] $$u^* + H_2O \rightarrow u + H_2O^* \text{ (physical deactivation by collision)}.$$

Equation [2] may represent several reactions, in which case k_2 will be the weighted mean rate constant for all the irreversible chemical processes. Reactions [1] and [2] are the only processes leading to a decrease in the concentration of uracil. Thus the total initial rate of disappearance of uracil will be $k_1.[u^*]_0[H_2O] + k_2[u^*]_0$ or, since the rates of reactions [1] and [2] are known to be roughly equal, we may represent the total initial rate approximately as $2k_1.[u^*]_0[H_2O]$.

In the presence of HCN we will have additional chemical reactions which may be lumped together as:

[4] $$u^* + HCN \xrightarrow{k_4} u.HCN \text{ (irreversible chemical reaction)}$$

where k_4 represents the weighted mean rate constant for the various reactions of u^* and HCN. We may neglect any effect of HCN on the purely physical processes of energy transfer for the concentrations of HCN employed in these experiments and, since this is still the principal mode of deactivation, the chemical quantum yields being of the order 0.01 mole per einstein, we may assume that $[u^*]_0$ will be essentially unchanged by the addition of the HCN. The initial rate of disappearance of uracil in the presence of HCN will therefore be $k_4[u^*]_0[HCN] + 2k_1.[u^*]_0[H_2O]$.

The ratio of the initial rates with and without HCN is:

$$\frac{k_4[u^*]_0[HCN]+2[k_1][u^*]_0[H_2O]}{2k_1[u^*]_0[H_2O]} = 1 + \frac{k_4[HCN]}{2k_1[H_2O]}.$$

In the experimental section the initial rate of disappearance of uracil during irradiation in the presence of 0.05 *M* HCN was found to be about 2.4 times the rate without HCN (Fig. 1), i.e.,

$$(k_4[0.05])/(2k_1[55.5]) = 1.4,$$

whence

$$k_4/k_1 = \text{ca. } 3100.$$

Even making allowance for the approximations involved in this derivation it appears that k_4 is larger than k_1 by a factor of the order of 10^3. This could explain the fact that the formation of the "reversible" product, 6-hydroxyhydrouracil, is almost completely suppressed in the presence of 0.05 *M* HCN.

CONDUCTANCE IN THE RANGE OF MEDIUM CONCENTRATION[1]

A. N. Campbell and R. J. Friesen

ABSTRACT

Equivalent conductances, densities, and viscosities of aqueous solutions of ammonium nitrate, of silver nitrate, and of lithium nitrate were determined at 25° C and at 35° C at concentrations ranging from 0.01 *N* to 1.0 *N*.

Experimental equivalent conductances have been compared with those calculated by the Wishaw–Stokes and Falkenhagen–Leist equations. Suitable choice of one parameter, the distance of closest approach, permits reproduction of the experimental data with an error of less than 0.5%. A study of the deviations of the calculated from the experimental conductances reveals that the distance of closest approach (so-called) varies appreciably with concentration and temperature.

In previous papers from this laboratory, we have reported our experimental results on conductances, densities, and viscosities of concentrated solutions (1). More recently, we have ventured into the field of extreme dilution (2). In the concentrated region, we have always compared our experimental results for equivalent conductance with the values calculated by means of the equations of Wishaw and Stokes (3) and of Falkenhagen and Leist (4); it is therefore not necessary to reproduce here these often-quoted equations. In the region of high concentration, the agreement between observed and calculated results is far from exact, and this is to be expected since neither of the above equations makes any assumptions other than those of the Debye–Hückel–Onsager treatment, and it is hardly to be expected that this relatively simple treatment would account for the behavior of the (presumably) complicated concentrated solutions.

We therefore decided to determine, with a high degree of accuracy, the conductances, densities, and viscosities, in a range of concentration varying from 0.01 *N* to 1.0 *N*, of those electrolytes with which much of our previous work has been done, viz. ammonium nitrate, silver nitrate, and lithium nitrate. The presumption was that agreement between calculated and observed conductances would be much better if the above equations have even approximate validity. We worked at the two temperatures, 25° C and 35° C. Our technique has been described frequently and need not be repeated here. The conductances of ammonium nitrate were corrected for hydrolysis by the method of Campbell and Bock (2); in the most dilute solution the correction amounts to 0.11 mho.

EXPERIMENTAL RESULTS

The experimental results are given in Tables I to VI. Three fundamental properties (density, specific conductance, and relative viscosity) and two derived properties (equivalent normality or molarity and equivalent conductance) are given for each solution.

DISCUSSION OF RESULTS

The densities are accurate to 0.002%, weight per cent concentration to 0.01%, and hence equivalent concentration to 0.015%. The accuracy of specific conductance measurements depends principally on the knowledge of the cell constant and this is known within 0.02%. Hence, equivalent conductances are within ±0.05% of their true values.

[1]*Manuscript received May 1, 1959.*
Contribution from the Department of Chemistry, University of Manitoba, Winnipeg, Manitoba.

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TABLE I

Data for ammonium nitrate solutions

At 25.00° C					At 35.00° C				
Concn. (mole/l.)	Density (g/ml)	Specific conductance (mho/cm $\times 10^6$)	Equiv. conductance (mho)	Rel. viscosity	Concn. (mole/l.)	Density (g/ml)	Specific conductance (mho/cm $\times 10^6$)	Equiv. conductance (mho)	Rel. viscosity
0.009893	0.99740	1350.9	136.47	0.999	0.009864	0.99439	1616.0	163.73	0.999
0.020033	0.99776	2671.8	133.32	0.998	0.019972	0.99472	3192.9	159.78	0.999
0.029175	0.99801	3830.7	131.26	0.998	0.029087	0.99498	4577.8	157.31	0.999
0.039970	0.99839	5170.5	129.33	0.997	0.039851	0.99540	6177.1	154.94	0.998
0.047956	0.99866	6146.3	128.13	0.996	0.047808	0.99559	7341.2	153.49	0.997
0.050005	0.99872	6395.0	127.86	0.998	0.049851	0.99566	7637.5	153.14	0.998
0.059997	0.99901	7601.0	126.66	0.996	0.059813	0.99594	9073.9	151.65	0.998
0.070046	0.99938	8792.6	125.50	0.997	0.069828	0.99628	10495.5	150.28	0.998
0.079920	0.99967	9955.0	124.54	0.996	0.079673	0.99658	11880.9	149.08	0.997
0.089968	1.00003	11130.3	123.70	0.996	0.089684	0.99687	13280.7	148.04	0.997
0.10001	1.00036	12285.5	122.83	0.995	0.099691	0.99720	14661.3	147.03	0.998
0.15363	1.00208	18344	119.39	0.993	0.15315	0.99894	21863	142.73	0.996
0.20090	1.00360	23529	117.10	0.990	0.20026	1.00041	28020	139.89	0.995
0.30230	1.00684	34302	113.46	0.986	0.30130	1.00353	40792	135.37	0.992
0.39993	1.00990	44327	110.83	0.982	0.39859	1.00650	52637	132.04	0.992
0.49647	1.01296	53993	108.74	0.977	0.49478	1.00951	64031	129.40	0.988
0.59710	1.01613	63832	106.90	0.975	0.59498	1.01251	75588	127.03	0.987
0.69976	1.01937	73640	105.23	0.973	0.69727	1.01575	87124	124.94	0.987
0.79943	1.02246	82966	103.77	0.968	0.79655	1.01877	98031	123.06	0.984
0.90237	1.02566	92510	102.51	0.967	0.89905	1.02189	109146	121.39	0.984
0.99976	1.02868	101306	101.32	0.963	0.99578	1.02458	119441	119.94	0.982

TABLE II

Data for silver nitrate solutions

At 25.00° C					At 35.00° C				
Concn. (mole/l.)	Density (g/ml)	Specific conductance (mho/cm $\times 10^6$)	Equiv. conductance (mho)	Rel. viscosity	Concn. (mole/l.)	Density (g/ml)	Specific conductance (mho/cm $\times 10^6$)	Equiv. conductance (mho)	Rel. viscosity
0.010156	0.99842	1267.0	124.75	1.001	0.010127	0.99549	1519.5	150.04	1.002
0.019394	0.99981	2354.2	121.39	1.003	0.019335	0.99678	2824.9	146.10	1.003
0.029459	1.00125	3503.3	118.92	1.004	0.029369	0.99820	4199.9	143.00	1.004
0.039998	1.00278	4675.2	116.89	1.004	0.039873	0.99966	5604.3	140.55	1.004
0.049659	1.00411	5720.5	115.20	1.003	0.049507	1.00104	6854.4	138.45	1.005
0.058313	1.00530	6643.7	113.93	1.003	0.058136	1.00224	7958.2	136.89	1.005
0.068343	1.00675	7691.4	112.54	1.004	0.068130	1.00362	9212.8	135.22	1.007
0.080014	1.00842	8895.5	111.18	1.005	0.079763	1.00526	10652.4	133.55	1.007
0.089961	1.00978	9902.2	110.07	1.005	0.089681	1.00663	11858	132.23	1.008
0.10063	1.01127	10968.2	109.00	1.005	0.10032	1.00811	13143	131.01	1.008
0.14915	1.01809	15655	104.96	1.008	0.14867	1.01485	18738	126.04	1.011
0.19797	1.02494	20148	101.77	1.011	0.19734	1.02167	24108	122.16	1.016
0.29997	1.03920	28982	96.62	1.016	0.29899	1.03580	34657	115.91	1.022
0.39976	1.05316	37051	92.68	1.022	0.39842	1.04961	44288	111.16	1.029
0.55271	1.07455	48674	88.06	1.027	0.55080	1.07082	58120	105.52	1.037
0.59523	1.08033	51646	86.77	1.030	0.59314	1.07654	61665	103.96	1.038
0.69928	1.09476	58860	84.17	1.038	0.69679	1.09087	70246	100.81	1.050
0.79154	1.10758	64962	82.07	1.046	0.78873	1.10364	77488	98.24	1.058
0.89509	1.12196	71594	79.99	1.053	0.89180	1.11783	85278	95.63	1.066
1.00088	1.13649	77977	77.91	1.062	0.99713	1.13225	92985	93.25	1.076

If $\mathring{a}$, the distance of closest approach in angstroms, is treated as the unknown in the equations of Falkenhagen–Leist and Wishaw–Stokes, it is possible to solve for this quantity, and to plot it as a function of concentration. This has been done in Figs. 1, 2, and 3, which are typical of many similar diagrams. In Fig. 1, $\mathring{a}$ of the Falkenhagen–Leist

TABLE III

Data for lithium nitrate solutions

At 25.00° C					At 35.00° C				
Concn. (mole/l.)	Density (g/ml)	Specific conductance (mho/cm $\times 10^6$)	Equiv. conductance (mho)	Rel. viscosity	Concn. (mole/l.)	Density (g/ml)	Specific conductance (mho/cm $\times 10^6$)	Equiv. conductance (mho)	Rel. viscosity
0.010572	0.99751	1083.0	102.44	1.000	0.010540	0.99446	1306.2	123.93	1.000
0.021061	0.99793	2105.4	99.97	0.999	0.020996	0.99485	2534.9	120.73	1.002
0.029775	0.99830	2920.0	98.07	1.004	0.029683	0.99523	3525.9	118.79	1.003
0.038848	0.99866	3770.3	97.05	1.005	0.038729	0.99559	4540.1	117.23	1.006
0.050821	0.99897	4861.3	95.66	—	0.050664	0.99589	5848.5	115.44	—
0.059158	0.99949	5604.1	94.73	1.007	0.058975	0.99640	6745.2	114.37	1.008
0.069872	0.99991	6533.8	93.51	1.009	0.069654	0.99679	7861.2	112.86	1.010
0.076234	1.00010	7095.4	93.07	1.008	0.075999	0.99700	8531.6	112.26	1.008
0.091701	1.00079	8448.0	92.13	1.011	0.091418	0.99770	10157.2	111.11	1.012
0.10111	1.00112	9247.6	91.46	1.011	0.10079	0.99798	11114.3	110.27	1.014
0.14980	1.00332	13290	88.72	1.017	0.14929	0.99997	15960	106.91	1.020
0.19937	1.00506	17267	86.61	1.022	0.19874	1.00186	20724	104.28	1.024
0.29918	1.00902	24887	83.19	1.043	0.29821	1.00576	29822	100.00	1.044
0.39900	1.01293	32130	80.53	1.042	0.39769	1.00960	38460	96.71	1.045
0.45941	1.01532	36341	79.10	1.050	0.45787	1.01192	43479	94.96	1.055
0.58142	1.02009	44546	76.62	1.060	0.57945	1.01662	53234	91.87	1.066
0.71135	1.02509	52771	74.18	1.075	0.70889	1.02154	62994	88.86	1.081
0.81640	1.02930	59193	72.51	1.087	0.81351	1.02566	70605	86.79	1.094
0.91191	1.03301	64745	71.00	1.098	0.90862	1.02929	77198	84.96	1.106
1.00464	1.03667	69959	69.64	1.114	1.0010	1.03287	83338	83.26	1.117

TABLE IV

Ammonium nitrate solutions at 25° C

I	II	III	IV	V	VI
0.01	136.47	136.4	136.61	136.59	136.5
0.02	133.32	133.0	133.54	133.51	133.4
0.03	131.26	131.0	131.56	131.50	—
0.04	129.33	128.9	129.69	129.62	129.4
0.048	128.13	127.7	128.52	128.44	128.2
0.05	127.86	127.6	128.24	128.15	—
0.06	126.66	126.1	126.99	126.89	126.6
0.07	125.50	125.1	125.89	125.78	125.4
0.08	124.54	124.0	124.90	124.78	—
0.09	123.70	123.2	123.99	123.85	123.4
0.10	122.82	122.3	123.15	123.01	—
0.15	119.39	118.6	119.59	119.38	—
0.2	117.10	116.0	117.19	116.95	115.9
0.3	113.46	111.8	113.46	113.14	—
0.4	110.83	108.9	110.83	110.45	—
0.5	108.74	106.2	108.78	108.35	106.1
0.6	106.90	104.3	107.08	106.56	—
0.7	105.23	102.4	105.56	105.04	—
0.8	103.77	100.5	104.34	103.77	100.4
0.9	102.51	99.1	103.23	102.63	—
1.0	101.32	97.6	102.30	101.68	97.7

NOTE: Column

I Gives the rounded concentration, moles per liter.

II Experimental equivalent conductance.

III Experimental equivalent conductance multiplied by relative viscosity.

IV Equivalent conductance calculated by Falkenhagen equation, $\mathring{a}$ = 2.625 Å.

V As for IV, except $\mathring{a}$ = 2.560 Å.

VI Equivalent conductance, calculated by Robinson–Stokes equation, with $\mathring{a}$ = 2.75 Å.

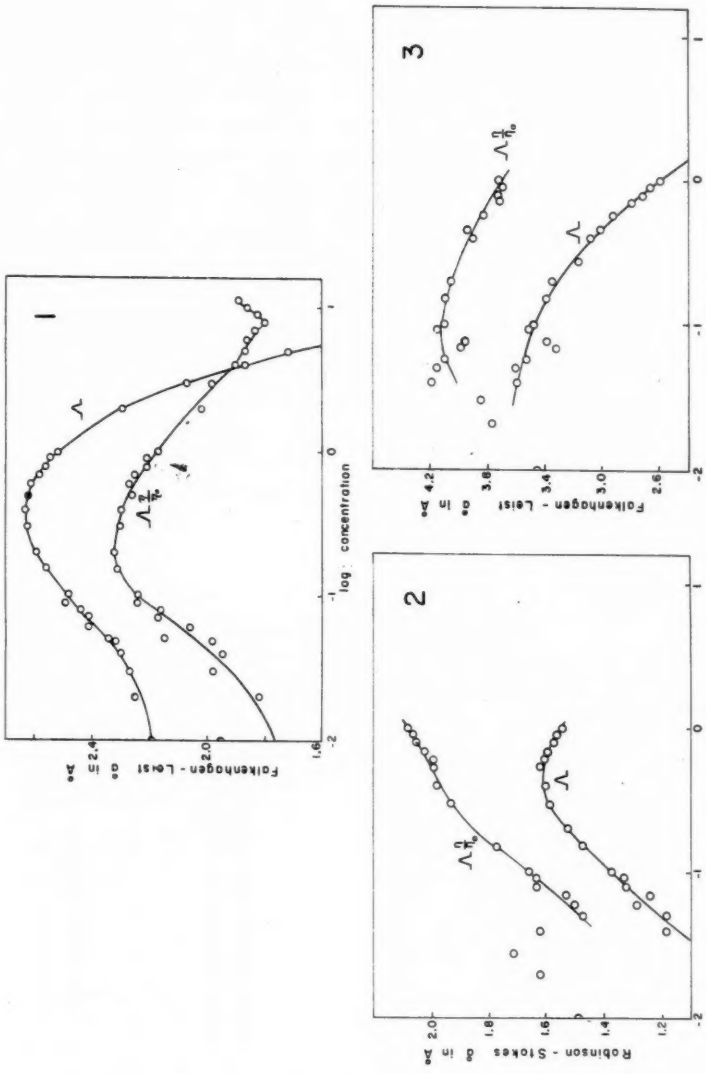

FIG. 1. δ(F–L) vs. log c, NH_4NO_3 at 25° C.

FIG. 2. δ(R–S) vs. log c, $AgNO_3$ at 25° C.

FIG. 3. δ(F–L) vs. log c, $LiNO_3$ at 25° C.

TABLE V

Silver nitrate solutions at 25° C

I	II	III	IV	V	VI	VII
0.01	124.75	124.7	124.70	124.8	124.68	124.8
0.02	121.39	121.7	121.65	121.9	—	121.9
0.03	118.92	119.4	119.22	119.7	119.28	119.6
0.04	116.89	117.3	117.14	117.6	117.20	117.6
0.05	115.20	115.5	115.53	116.0	115.60	116.1
0.06	113.93	114.3	114.23	114.8	114.32	115.1
0.07	112.54	113.0	112.90	113.5	112.97	113.6
0.08	111.18	111.7	111.49	112.2	111.54	112.3
0.09	110.07	110.6	110.37	111.1	110.42	111.3
0.10	109.00	109.6	109.26	110.1	109.33	110.3
0.15	104.96	105.8	105.08	106.2	105.17	106.4
0.2	101.77	102.9	101.75	103.0	101.82	103.3
0.3	96.62	98.1	96.39	98.2	96.43	98.4
0.4	92.68	94.7	92.40	94.6	92.37	94.9
0.55	88.06	90.4	87.58	90.4	87.53	90.5
0.6	86.77	89.4	86.47	89.5	86.37	89.6
0.7	84.17	87.4	83.99	87.3	83.81	87.2
0.8	82.07	85.8	82.02	85.5	81.81	85.4
0.9	79.99	84.2	80.07	83.9	79.79	83.7
1.0	77.91	82.7	78.27	82.4	77.91	82.0

NOTE: Column

I Rounded concentration, moles per liter.

II Experimental equivalent conductance.

III Experimental equivalent conductance multiplied by relative viscosity.

IV Calculated equivalent conductance, Falkenhagen equation, $\mathring{a}$ = 1.51 Å.

V Same as IV, except $\mathring{a}$ = 1.80 Å.

VI Calculated equivalent conductance, Robinson–Stokes, $\mathring{a}$ = 1.54 Å.

VII Same as VI, except $\mathring{a}$ = 2.00 Å.

TABLE VI

Lithium nitrate solutions at 25° C

I	II	III	IV	V
0.01	102.44	102.4	102.31	102.6
0.02	99.97	99.9	99.57	100.1
0.03	98.07	98.5	97.94	98.6
0.04	97.05	97.5	96.57	97.3
0.05	95.66	96.2	95.05	96.1
0.06	94.73	95.4	94.11	95.3
0.07	93.51	94.4	93.07	94.4
0.08	93.07	93.9	92.51	94.0
0.09	92.13	93.1	91.30	92.9
0.10	91.46	92.5	90.57	92.3
0.15	88.72	90.3	87.80	90.1
0.2	86.61	88.5	85.76	88.3
0.3	83.19	86.7	82.43	85.9
0.4	80.53	83.9	80.11	84.2
0.5	79.10	83.1	78.98	83.4
0.6	76.62	81.2	77.11	82.0
0.7	74.18	79.7	75.48	81.2
0.8	72.51	78.9	75.17	—
0.9	71.00	78.0	—	—
1.0	69.64	77.6	—	—

NOTE: Column

I Rounded concentration, moles per liter.

II Experimental equivalent conductance.

III Experimental equivalent conductance multiplied by relative viscosity.

IV Calculated equivalent conductance, Falkenhagen equation, $\mathring{a}$ = 3.00 Å.

V Same as IV, except $\mathring{a}$ = 4.00 Å.

equation, for ammonium nitrate at 25° C, is plotted against log c; one curve refers to equivalent conductance without viscosity correction, the other to conductance multiplied by relative viscosity. In Fig. 2, the $\mathring{a}$ of the Wishaw–Stokes equation, for silver nitrate at 25° C, is plotted against log c. In Fig. 3, the Falkenhagen–Leist $\mathring{a}$, for lithium nitrate, is plotted against log c. It is apparent that $\mathring{a}$ is far from constant; often it appears to pass through a maximum. Theoretically, $\mathring{a}$ should be independent of concentration and even, perhaps, of temperature. In fairness, however, it should be pointed out that this method of treatment forces $\mathring{a}$ to absorb not only all the imperfections in the conductance equations but any experimental error as well.

Considering the Falkenhagen–Leist equation only, it appears that $\mathring{a}$ determinations in dilute solutions show greater scatter than in concentrated solutions. The reason for this is that $\mathring{a}$ appears only in the linear and quadratic divisors $(1+Ka)$ and $(1+1/2\sqrt{2}Ka+1/6K^2a^2)$, both of which approach unity with dilution. The more dilute the solution, the greater the uncertainty in the determination of $\mathring{a}$ from conductance.

Curves similar to Figs. 1, 2, and 3, for the higher temperature (35° C), show that above 0.1 N there is no doubt that two different $\mathring{a}$ values are necessary to reproduce the experimental results at the two temperatures.

Despite the apparent variations in $\mathring{a}$, however, if a suitable "best" value of $\mathring{a}$ is chosen, it is possible to reproduce the values of equivalent conductance, between 0.01 N and 1.0 N, within 0.5 mho, using either the Falkenhagen–Leist or the Wishaw–Stokes equation. This is shown in Tables IV, V, and VI, which are self-explanatory. Although it might seem that, on theoretical grounds, the Wishaw–Stokes equation is less acceptable than that of Falkenhagen–Leist, the agreement between calculation and experiment is better with the former equation: this we have observed before.

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LIGHT ABSORPTION STUDIES

PART XIV. THE ULTRAVIOLET ABSORPTION SPECTRA OF PHENOLS[1]

J. C. Dearden and W. F. Forbes

ABSTRACT

A spectral analysis of benzene derivatives is extended to substituted phenols. The discussion emphasizes hydrogen bonding and steric effects which occur in phenols. Some of the phenolic absorption bands are ascribed to locally excited states.

INTRODUCTION

The effect of the hydroxy group on the electronic spectra of benzene derivatives is of interest for a number of reasons. First, phenols are known to give rise to various forms of hydrogen bonding, and hence the investigation of spectral effects which may be ascribed to hydrogen bonding affords further information concerning the nature of the hydrogen bond. Next, compounds which may be regarded as substituted phenols, for example flavones, frequently occur as natural products, and hence an understanding of phenolic spectra assists in the identification and quantitative estimation of such naturally occurring compounds. Lastly, previous papers in this series have attempted to analyze the spectra of benzene derivatives in terms of mesomeric and steric interactions, and it is therefore of interest to test these hypotheses on the observed spectra of phenols.

The ultraviolet spectra of a number of phenols have previously been investigated by other workers (1, 2, 3, 4, 5), but whenever convenient we have redetermined the spectra in order to ensure near-identical conditions.

THE SPECTRUM OF PHENOL

Phenols generally exhibit two absorption bands in the spectral region under investigation, that is, between 200 and 360 mμ. The band at longer wavelength is referred to as the *C*-band, and the band at shorter wavelength as the *B*-band. This assignment corresponds to the assignment for anilines and is based on similar reasoning (cf. ref. 6). The data for phenol are listed in Table I.

The bands are somewhat altered with change of solvent, and it has been shown by Coggeshall and Lang (3) that some of these spectral changes do not depend on *stable* hydrogen-bonded complexes, although there is evidence that some of the observed spectral changes are caused by some type of hydrogen bonding (5). Various forms of intermolecular hydrogen bonding are certainly possible, involving both the hydrogen atom of the hydroxy group and the oxygen atom. The wavelength displacement between the spectra in the vapor phase and in cyclohexane solution must also result from some solute–solvent interaction; but the latter interaction is unlikely to be associated with hydrogen bonding because similar displacements are observed for phenols and anilines (cf. ref. 6). In more concentrated solutions of phenol in cyclohexane, yet other spectral effects occur, presumably caused by intermolecular hydrogen bonding between phenol molecules (see ref. 4).

The fine structure of the *C*-band for phenol or anisole in cyclohexane or similar inert media is fairly characteristic of these chromophores, and can often be recognized in substituted, including sterically hindered, phenols (see also later section). The fine structure disappears if the phenolic species no longer contributes appreciably to the

[1]*Manuscript received November 10, 1958.*
Contribution from the Memorial University of Newfoundland, St. John's, Newfoundland.

TABLE I

Absorption maxima of phenol in various solvents

(Values in italics represent inflections in this and subsequent tables)

Solvent	*B*-Band		*C*-Band		Source
	$\lambda_{max}(m\mu)$	ϵ_{max}	$\lambda_{max}(m\mu)$	ϵ_{max}	
Vapor phase	205	†	261 264 266.5 *ca. 270* 273	†	*
Cyclohexane (*B*-band concn. = 2.3×10^{-4} moles/l.)	210	6000	263 269 276	1400 2200 2100	*
Ether	218	6400	266 271 277.5	1600 2200 1800	*
Ethanol	218.5	6000	*ca. 266* 271 *276*	*1500* 1900 *1450*	*
Water	210	6000	268 *273*	1500 *1250*	*
0.1 *N* HCl	210	6000	268 *273*	1600 *1300*	*
N NaOH	234	10500	285	2700	*
Conc. H_2SO_4	231.5	9500	261 *ca. 271* 278–279	830 *980* 1150	*

*This series of papers. †Intensities not determined.

observed spectrum; as for example in the *C*-band of *m*-nitro- or *m*-amino-phenol, where the compound absorbs preferentially as nitrobenzene or aniline (see Table II). The fine structure of the *C*-band also disappears for intramolecularly hydrogen-bonded molecules such as salicylaldehyde (see Table II), but the fine structure *is* noticeable for a number of orthosubstituted phenols even in ethanolic solution (see Table III). The most probable explanation seems to be that this fine structure is caused by vibrational sublevels and that a hydrogen bond may obscure this fine structure. Hence, the fine structure is frequently reduced if the phenol is associated with a solvent molecule by means of an intermolecular hydrogen bond (see Table I) or if the phenol molecule is intramolecularly hydrogen-bonded, but the fine structure does become evident if steric interactions hinder the formation of a hydrogen bond (see section on orthosubstituted phenols).

In sodium hydroxide solution the phenolic spectrum is radically altered, and the spectrum is assumed to correspond to the phenolate ion. For phenol in basic medium, compared with cyclohexane solution, a wavelength displacement of 24 mμ is observed for the *B*-band and a displacement of 16 mμ is observed for the *C*-band (see Table I). As expected, similar wavelength displacements are not observed for the spectrum of anisole (see ref. 7).

THE SPECTRA OF PARASUBSTITUTED PHENOLS

The spectra of substituted phenols are listed in Table II.

Table II lends support to the naming of the *B*-bands, that is, as bands corresponding to the so-called *B*-bands in benzene, acetophenone, nitrobenzene, benzoic acid, and

TABLE II

Absorption maxima of substituted phenols

		Para isomer				Meta isomer						Ortho isomer					
		B-Band		*C*-Band		Phenolic *B*-band		2nd *B*-band		*C*-Band		Phenolic *B*-band		2nd *B*-band		*C*-Band	
Substituent	Solvent	$\lambda_{max}(m\mu)$	ϵ_{max}	$\lambda_{max}(m\mu)$	ϵ_{max}	$\lambda_{max}(m\mu)$	ϵ_{max}	$\lambda_{max}(m\mu)$	ϵ_{max}	$\lambda_{max}(m\mu)$	ϵ_{max}	$\lambda_{max}(m\mu)$	ϵ_{max}	$\lambda_{max}(m\mu)$	ϵ_{max}	$\lambda_{max}(m\mu)$	ϵ_{max}
-OH	Cyclohexane	223	4400*	*ca. 285*	*2500**	*ca.217*	*6800**	—	—	*ca. 268*	*1650**	214	6800	—	—	*ca. 270*	*2200*
				289	2800					273.5	2150					274	2500
				292	2900					279.5	1800					280	2250
				ca. 299	*2200*												
-OCH_3	Cyclohexane	224	7000	*ca. 285*	*2900*			220	5400†	*ca. 267*	*1300*			216	6200†	*ca. 270*	*2250*
				288	3150					271.5	1650					273.5	2550
				291	3100					278	1550					279.5	2150
				298	2350												
-NH_2	Cyclohexane*	235	7150‡	304	2550‡			234	6800	284	2300			235	7000	288	3300
	Water	229	6100‡	294	2000‡			229	6400	278	1900			229	6150	281	2700
	pH 3 or 0.1 *N* HCl	218.5	6240§	262.5	1450§	217	6300	*ca. 212*	*6150†*	269	1900	210	6500†			268	2100
										ca. 273	*1700*					*ca. 273*	*1800*
-CH_3	Cyclohexane	220	5900	268	1400	214	6100			271	1600	213	7000			270	1850
				271.5	1600					277	1850					276	1750
				274	1850												
				277	2150												
				283.5	1950												
-C_2H_5	Cyclohexane	221	7250	*ca. 267*	*1400*							212	7450			*ca. 263*	*1400*
				270	1600											270	2000
				273	1800											276	1900
				276	2200												
				282	2000												
-$CH(CH_3)_2$	Cyclohexane	220	6850	*ca. 267*	*1350*							211	7500			*ca. 264*	*1500*
				ca. 270	*1500*											270	2100
				ca. 272	*1700*											276	2000
				275	2100												
				281	1900												
-$C(CH_3)_3$	Cyclohexane	219	6800	*ca. 268*	*1500*							213	5900			*ca. 263*	*1400*
				274	2100											268.5	2050
				280	2050											275	2100

TABLE II (*Concluded*)

Absorption maxima of substituted phenols

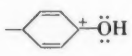
		Para isomer				Meta isomer						Ortho isomer					
		B-Band		*C*-Band		Phenolic *B*-band		2nd *B*-band		*C*-Band		Phenolic *B*-band		2nd *B*-band		*C*-Band	
Substituent	Solvent	λ_{max}(mμ)	ϵ_{max}	λ_{max}(mμ)	ϵ_{max}	λ_{max}(mμ)	ϵ_{max}	λ_{max}(mμ)	ϵ_{max}	λ_{max}(mμ)	ϵ_{max}	λ_{max}(mμ)	ϵ_{max}	λ_{max}(mμ)	ϵ_{max}	λ_{max}(mμ)	ϵ_{max}
-F	Cyclohexane	210–211	4200	267	1700	211.5	5200			*ca. 262*	*1150*	212	5800			262	1250
				269.5	2200					266.5	1450					266	1600
				272.5	2500					272	1300					272	1400
				275.5	2750												
				278.5	3100												
				ca. 282	*2000*												
				285	2600												
-Cl	Cyclohexane	224	8800	*ca. 273*	*1400*	216	6500			266	1300	212	6450			*ca. 265*	*1550*
				279	1850					272	2050					271	2350
				287	1700					279	2000					278	2450
-Br	Cyclohexane	224	10250	*ca. 273*	*1300*	210	7500†			266	1450	212	8700			*ca. 266*	*1750*
				279.5	1750	*215*	*7000*			272	2300					272	2700
				287	1500					279	2250					279	2650
-I	Cyclohexane	230.5	15000	273.5	1300									218	9250†	268	2200
		ca. 235	*12400*	279.5	1450									224	8300	274	3000
				288	1100									229	6500	281.5	2800
-CHO	*n*-Hexane	265–266	19000	—	—	213	19000†	244	10000	302	2900	215	17000†	250	11000	324–325	3600
		ca. 274	*15500*					250	9500	*ca. 307*	*2800*			257	11700		
		281	12000†														
		288	6000†														
	0.1 *N* NaOH	330	27900§	—	—§	237	23900‖	267	6200‖	357	2600‖	226.5	18200‖	264.5	7500‖	377	6700‖
$-NO_2$	Cyclohexane	295	11300*	—	—*	225	11000*	262	5750*	319	2150*	*ca. 230*	*4000*	269	7350	342	3700
	Water	313–314	9300	—	—	228	7650	272	5950	328	1950	*ca. 250*	*3700*	276	6350	346	3050
	0.1 *N* or *N* NaOH	402.5	19200§	—	—§	251.5	11000‖	291	4500‖	392	1500‖	*250*	*6000‖*	282	4300‖	416	4800‖
-COOH	Cyclohexane	251	15000	—	—			235–236	6500	296	2900			237–238	8000	307	4400
	Ethanol	253–254	15000	—	—			234–235	6000	301	2300			236	7500	307	3700

*In cyclohexane containing *ca.* 2% ether. †*B*-Band assignment doubtful. ‡Aniline absorption. §Ref. 8. ‖Ref. 9.

benzaldehyde, although the excited state of phenol may represent a locally excited state (see below). This follows because the gradual displacement of the band for a series of compounds such as phenols indicates that the main absorption band in phenol (and incidentally aniline) is of similar nature for the compounds listed in Table II. Further, as shown in Parts XI and XII (10, 11), this same band, for example in *p*-hydroxyacetophenone, can likewise be related to the *B*-band in acetophenone. This confirms the suggestion that *all* the above-mentioned absorption bands may be described as *B*-bands.*

The *B*-band in phenol is shown to be displaced to longer wavelength on parasubstitution. If the parasubstituent is electron-withdrawing, this displacement is greater, *qualitatively* related to the electron-withdrawing effect of the substituent, and the usual high-intensity band corresponding to an extended conjugated system is obtained. The wavelength displacements with respect to phenol in cyclohexane are parallel to the displacements in the aniline series (6). The *quantitative* relation observed between spectra of parasubstituted nitrobenzenes, acetophenones, and benzaldehydes (10, 11) is, however, absent for the displacements observed between parasubstituted anisoles and phenols, since in the latter example the straight line plot of the wavelength displacements does not pass through the origin (see following paper).

As will also be shown in the following paper and elsewhere, this difference can be rationalized by assuming that the *B*-band in phenol involves transitions which should be associated to an appreciable extent with locally excited states of type I. In support of this hypothesis the following may be cited: (i) the *B*-band of phenol at 210 mμ in



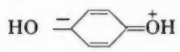
I

II

cyclohexane is displaced by about 7 mμ from the corresponding band in benzene, a wavelength displacement similar to that associated with the short-range interaction of the hydroxy group (see section on metasubstituted phenols); (ii) if phenol is assumed to absorb at longer wavelength, because hypothetical structures of type II contribute more appreciably to the electronic excited state, the above-mentioned relationship between wavelength displacements in parasubstituted anisoles and phenols becomes more nearly quantitative (see following paper); (iii) steric effects in the *B*-band of phenol are different from those which would be anticipated for a band associated with transitions to excited states of type II (see section on orthosubstituted phenols); (iv) the anomalous nature of the wavelength displacements for phenols has previously been noted by Doub and Vandenbelt (8); and (v) the bathochromic wavelength displacement obtained for the spectra of metasubstituted phenols compared with the spectrum of phenol when the metasubstituent is electron-withdrawing can be explained since an electron-withdrawing substituent has been assumed to facilitate resonance forms of type II (see ref. 6) and this therefore can account for the anomalous *bathochromic* wavelength displacement (see the discussion of the spectra of metasubstituted phenols).

**Alternatively, it has been proposed that the B-band of compounds like, for example, nitrobenzene should be related to the C-band of benzene, that is to the band occurring in benzene at ca. 250 mμ. Wepster (12), in the course of a discussion on steric effects, suggests that this latter argument is supported because for sterically hindered nitrobenzenes the absorption band in hexane remains near 250 mμ, that is, near the C-band absorption of benzene. Our interpretation is to regard this band in substituted nitrobenzenes as a nitrobenzene B-band, since the latter band also occurs near 250 mμ. We believe that our argument receives support from the absorption maxima of sterically hindered p-nitroanilines in ethanol. These maxima are all reported to occur near 380 mμ (12), that is, near the maximal absorption of p-nitroaniline, and the maxima for these examples do not therefore revert to a maximum near 250 mμ.*

It may be noted that this hypothesis assumes that the absorption of parasubstituted phenols such as *p*-cresol, hydroquinone, or *p*-bromophenol may still involve locally excited states of type I with both substituents exerting only a secondary effect. However, in compounds of this type, structures involving appreciable resonance interaction with at least one substituent seem more probable because the second substituent facilitates additional electronic interaction. The relevant structures may be represented by resonance forms of types III and IV, and consideration of structure IV also suggests that structure



III

IV

V

V cannot be ruled out. The actual contributing structures will depend on the relative over-all electronegativities of the two substituents in the ground and excited states. For phenols in basic media, a different type of resonance interaction presumably occurs in the excited state because of the replacement of the phenol group by the phenolate ion. Since this resonance interaction will be reflected in the maximal wavelengths it follows that the mesomeric interaction between the hydroxy group and the benzene ring is less than the mesomeric interaction between the amino group and the benzene ring. Extending the argument one step further, the maximal absorptions suggest an order of mesomeric interaction $PhO^- > PhNH_2 > PhOH > PhNH_3^+$.

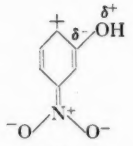
The *C*-band shows the expected changes if the parasubstituent is electron-withdrawing, namely, with increase of mesomeric interaction the *C*-band usually becomes progressively less pronounced (see Table II and Ref. 13). If the parasubstituent is electron-donating, the fine structure of the *C*-band is frequently enhanced, the effect being most pronounced for the spectra of *p*-methyl- and *p*-fluoro-phenol in cyclohexane. It is worth noting that the fine structure of the *C*-band in these latter compounds is considerably more pronounced than for the corresponding meta isomers (see Table II). This is surprising since increased molecular symmetry is generally assumed to simplify the absorption spectra, and one would therefore have expected the fine structure of the *C*-band to be less pronounced in the para isomer than in the meta isomer.

THE SPECTRA OF METASUBSTITUTED PHENOLS

In metadisubstituted benzene derivatives direct resonance interaction is ruled out by definition, and hence we would expect two *B*-bands corresponding to the two monosubstituted benzene derivatives (cf. refs. 6, 10, 11). Both these bands may be modified because of the other substituent, either by means of secondary short-range electronic interactions (cf. ref. 7), or possibly because of the buttressing effect (cf. refs. 14, 15). It is, of course, possible that one of the two *B*-bands may be obscured, either because of overlap by the other *B*-band or because of *A*-band absorption (cf. ref. 13), and these factors may also prevent a reliable band assignment for some examples. On the other hand, characteristic properties like the fine structure of the phenolic *C*-band assist in the band assignments.

These generalizations are illustrated for phenols in Table II. If the non-phenolic substituent is electron-withdrawing, it is found that the non-phenolic *B*-bands are normally displaced to longer wavelength on account of the secondary interaction of the hydroxy group, and this displacement is of the order of 7 mμ for a number of compounds (cf. ref. 7). This wavelength displacement of *ca.* 7 mμ suggests that the hydroxy group tends

to facilitate the absorption of the non-phenolic chromophore. The hypothesis may be illustrated by structures of type VI, by analogy with similar structures used in previous arguments (cf. ref. 10). In basic media the secondary interaction is considerably increased, because of the replacement of the hydroxy group by the O^--entity, and bathochromic wavelength displacements of up to 25 mμ (for *m*-nitrophenol compared with nitrobenzene) are observed.



VI

As has previously been noted by Lemon (2, cf. also ref. 7),* the effect of alkali on the spectra of hydroxybenzaldehydes and hydroxyacetophenones is greatest in the para isomers.

Our data also show that for the *B*-bands the displacement in the para isomers in basic media is much more pronounced. For example, the phenolic *B*-band of *m*-nitrophenol on passing from neutral to alkaline solution shows a wavelength displacement of 23.5 mμ (see Table II), comparable with the displacement of 24 mμ for phenol (see Table I). In the para isomer, presumably because appreciable primary resonance interaction occurs, the displacement of the *B*-band, caused by the addition of alkali, is *ca.* 90 mμ (see Table II). These observations may be of some practical importance. For example, if the *B*-band of an acetyl-substituted phenol on changing the solvent from neutral to basic medium does not show a bathochromic wavelength displacement greater than *ca.* 25 mμ, it may be assumed that no uninhibited, direct mesomeric interaction occurs between the hydroxy and acetyl groups.

The effect of the second substituent on the *phenolic B*-band is also illustrated for some of the compounds listed in Table II. Unfortunately, the relevant absorption band frequently occurs at too short a wavelength to be identified with certainty. However, for a few compounds the band assignment presents little difficulty, as for example, in *m*-nitrophenol where the phenolic absorption is appreciably displaced to longer wavelength (see Table II). This latter displacement has previously been ascribed to the nitrosubstituent facilitating the phenolic absorption (10). This bathochromic displacement for the phenolic *B*-band in compounds like *m*-nitrophenol may be related to the changes in the integrated absorption intensities for the infrared hydroxyl absorption in phenols, since the integrated absorption intensity for compounds like *m*-nitrophenol is greater than for phenol (17, 18), and since increased integrated absorption intensities, like bathochromic wavelength displacements in the *B*-band, may be related to increased mesomeric interactions.

It should be noted that when the metasubstituent is electron-withdrawing, the phenolic *B*-band appears sometimes to be moved to longer wavelength (see Table II), whereas the anilinic *B*-band under these conditions is moved to shorter wavelength (see ref. 6). More-

**Lemon arrives at this conclusion, although for the ortho and meta isomers he considers what we believe to be the C-band, whereas for the para isomers he considers the B-band. Another example of what we believe is an incorrect assignment is provided by the reported data for the intense o-hydroxyacetophenone band near 315–330 mμ, which has been described as a B-band (K-band, see ref. 16), whereas we would regard it as a displaced C-band.*

over, these wavelength displacements are parallel in the corresponding infrared bands. For example, in *m*-nitroaniline compared with aniline (19), the NH_2 stretching vibration is moved to higher frequency, that is to shorter wavelength, whereas the OH stretching vibration in *m*-nitrophenol compared with phenol is moved to lower frequency. These anomalous wavelength displacements for phenols can be explained by assuming that the *B*-band of phenol occurs at unusually *short* wavelength because of the contribution of locally excited states of type I (see section on parasubstituted phenols). In this way, the above-mentioned comparisons involving phenol are rendered invalid, in the sense that metasubstituted phenols compared with hypothetical phenol molecules containing more similar contributions of locally excited states than aniline may still afford the anticipated hypsochromic wavelength displacement.

If the above assignments are accepted, examination of the relative intensities of the two *B*-bands suggests that the phenolic *B*-band absorption usually occurs preferentially. For example, in *m*-nitrophenol, compared with the two monosubstituted parent compounds, the nitrobenzene *B*-band absorption decreases, whereas the phenolic absorption increases in intensity. A similar relative intensity increase is observed for the aniline *B*-band in *m*-nitroaniline (6), although the relative increase in the intensity of the phenolic *B*-band is less than for the anilinic *B*-band. These observations may be rationalized by a converse of the mechanism postulated to account for the increased extinction coefficient in associated benzoic acid molecules (see ref. 20). There it was shown that an electron-withdrawing substituent, in the absence of direct resonance interaction, gives rise to an increased maximal extinction coefficient. Likewise, in metasubstituted anilines or phenols the nitro group may be assumed to increase the probability of the phenolic or anilinic transition, and conversely, the *m*-hydroxy and the *m*-amino substituents may be assumed to have the effect of relatively ***weakening*** the nitrobenzene absorption, the effects being more pronounced for the meta-amino substituent, which donates electrons more effectively.

Some of the *C*-bands in metasubstituted phenols show the expected changes. For example, if the metasubstituent is electron-withdrawing the *C*-bands are enhanced compared with the *C*-bands in para isomers (cf. ref. 13).

THE SPECTRA OF ORTHOSUBSTITUTED PHENOLS

The *B*-bands of the ortho isomers frequently resemble the *B*-bands of the meta isomers. For example, for *o*-nitrophenol in 0.1 *N* NaOH where intramolecular hydrogen bonding is ruled out, the nitrobenzene band at 282 mμ, $\epsilon = 4300$, is similar to the nitrobenzene *B*-band in the meta isomer which occurs at 291 mμ, $\epsilon = 4500$ (9). The phenolic *B*-band is considerably reduced in intensity and occurs in the ortho isomer as an inflection at 250 mμ, $\epsilon = 5000$, whereas in the meta isomer it occurs at 251.5 mμ, $\epsilon = 11{,}000$ (9, and see Table II). For *o*-nitrophenol in basic solution there is therefore no evidence for appreciable resonance interaction. Similar spectral effects are observed in other examples listed in Table II, and the examples of 2,4- or 2,4,6-substituted nitrobenzenes when an ortho-alkyl substituent does not contribute to the direct resonance interaction, have previously been mentioned in this paper in the discussion of parasubstituted phenols. Effects of this type may also be noted in the *B*-bands of a number of parasubstituted phenols in neutral solution when, on introduction of two *t*-butyl groups in the ortho-positions, no appreciable wavelength displacement is observed, but a decreased extinction coefficient indicative of steric interactions is obtained (21).

This absence of resonance interaction may be ascribed to steric interactions, and steric interactions are also indicated by a number of other physical properties, such as the decreased intermolecular hydrogen bond formation in sterically hindered phenols (3, 15, 22, cf. also 23), and more generally by the failure of sterically hindered phenols to exhibit normal phenolic properties (cf. for example, ref. 21). These observed steric effects may be associated, at least partly, with the two unshared electron pairs on the oxygen atom, since a steric effect caused entirely by the more distant hydrogen atom of the hydroxy group would not account satisfactorily for the observed steric effects (cf. ref. 24, p. 360). The *B*-band in orthosubstituted phenols does not normally undergo a pronounced wavelength displacement even if the orthosubstituents are bulky as in diortho-*t*-butylphenol (see Table III). The absence of this spectral effect, characteristic of steric inhibition of resonance in many other conjugated systems, has already received an explanation (see section on parasubstituted phenols, which tentatively ascribes the

TABLE III

Absorption maxima of orthosubstituted phenols in cyclohexane and ethanol

	Cyclohexane		Ethanol	
Orthosubstituents	λ_{max}(mμ)	ϵ_{max}	λ_{max}(mμ)	ϵ_{max}
H,H (*B*-Band)	210	6000	218.5	6000
H,H (*C*-Band)	263 269 276	1400 2200 2100	*ca. 266* 271 *276*	*1500* 1900 *1450*
H,CH_3 (*B*-Band)	213	7000	213	7100
H,CH_3 (*C*-Band)	270 276	1850 1750	272 *ca. 276*	2050 *1800*
H,$CH(CH_3)_2$ (*B*-Band)	211	7500	215	6200
H,$CH(CH_3)_2$ (*C*-Band)	*ca. 264* 270 276	*1500* 2100 2000	271 *ca. 276*	2250 *2000*
H,$C(CH_3)_3$ (*B*-Band)	213	5900	216	5100
H,$C(CH_3)_3$ (*C*-Band)	*ca. 263* 268.5 275	*1400* 2050 2100	271 277	2300 2050
CH_3,CH_3 (*B*-Band)	211–212	7900	*ca. 214*	*8500*
CH_3,CH_3 (*C*-Band)	269 275	1500 1600	271 *ca. 275*	1550 *1450*
$CH(CH_3)_2$,$CH(CH_3)_2$ (*B*-Band)	211	9200	*ca. 214*	*8000*
$CH(CH_3)_2$,$CH(CH_3)_2$ (*C*-Band)	269 275.5	1900 1950	270.5 *ca. 275*	1850 *1700*
$C(CH_3)_3$,$C(CH_3)_3$ (*B*-Band)	211	7500	*ca. 212*	*7600*
$C(CH_3)_3$,$C(CH_3)_3$ (*C*-Band)	268 275	1800 1800	268 274	1550 1500
H,Cl (*B*-Band)	212	6450	216	6400
H,Cl (*C*-Band)	*ca. 265* 271 278	*1550* 2350 2450	274.5 *ca. 280*	2350 *2000*
H,Br (*B*-Band)	212	8700	*ca. 214*	*8450*
H,Br (*C*-Band)	*ca. 266* 272 279	*1750* 2700 2650	275.5 *ca. 281*	2750 *2350*

phenolic absorption to transitions involving locally excited states). Steric interactions are, however, indicated in the ultraviolet spectra by the *absence* of the usual wavelength displacements between solutions in cyclohexane and ethanol. That is, whereas between solutions of phenol in cyclohexane and ethanol a wavelength displacement of 8 mμ is observed in the *B*-band (see Table I), no such displacement is observed for solutions of strongly sterically hindered phenols (see Table III for the spectra of various orthosubstituted phenols in cyclohexane and ethanol). Our explanation, following the suggestion of Coggeshall and Lang (3), is to ascribe a reduced wavelength displacement to steric interactions inhibiting solvent–solute interactions between phenol and solvent molecules.

Yet another spectral effect which may be associated with steric interactions is the progressive *increase* in extinction coefficient of the *C*-band for the spectra of orthosubstituted phenols in alkaline solution with increased size of the orthosubstituent (cf. ref. 13). The relevant *C*-band data are listed in Table IV, and Table IV also shows that the *B*-bands are not appreciably affected under these conditions.

TABLE IV

Absorption maxima of orthosubstituted phenols in alkaline solution (*N* aqueous NaOH)

	B-Band		*C*-Band	
Orthosubstituents	λ_{max}(mμ)	ϵ_{max}	λ_{max}(mμ)	ϵ_{max}
H,H	234	10500	285	2700
H,CH_3	235	9000	286	3200
H,C_2H_5	236	8400	287	3400
H,$CH(CH_3)_2$	236	8900	287	3700
CH_3,CH_3	238	8000	285	3400
$CH(CH_3)_2$,$CH(CH_3)_2$	238–239	8100	289	4550
$C(CH_3)_3$,$C(CH_3)_3$*	247–248	8300	292–293	4800

*Solution contains *ca.* 1% ethanol.

Next, in neutral solution, there is evidence for intramolecular hydrogen bonding, and the spectral effects ascribed to hydrogen bonding are more pronounced for orthosubstituted phenols than for the corresponding anilines (cf. ref. 6). The evidence is obtained by comparing the *B*-bands of a number of orthosubstituted phenols with the *B*-bands of the meta isomers, where the former *B*-bands show a bathochromic wavelength displacement accompanied by an increased absorption intensity.

Since these spectral changes are much more pronounced in orthosubstituted phenols than in the corresponding anisoles (see following paper) it is assumed that the spectral changes must be caused, at least partly, by intramolecular hydrogen bonding. Evidence for an intramolecular hydrogen bond in, for example, *o*-nitrophenol is also provided by the appreciably displaced hydroxyl band in the infrared region at 3240 cm^{-1} for *o*-nitrophenol compared with the band at 3590 cm^{-1} for the meta and para isomers (25, 26, cf. also refs. 27, 28, 29). Further evidence is provided by the C–H bending frequency at 748 cm^{-1} for *o*-nitrophenol (30).

EXPERIMENTAL

The ultraviolet absorption spectra were determined by standard methods using a Unicam SP500 spectrophotometer. For each compound at least two independent sets of observations were made. Some of the spectra have previously been described in this series.

The phenols were mostly commercial materials, purified by distillation or recrystallization until their boiling points or melting points showed them to be sufficiently pure. The solvents used were spectroanalyzed cyclohexane (Fisher) or commercially available absolute ethanol. The spectra of the aminophenols and dihydroxybenzenes were determined as quickly as possible to prevent oxidation. With this end in mind, the air in the flasks containing these solutions was also replaced by nitrogen.

ACKNOWLEDGMENTS

The authors are greatly indebted to Miss Florence Jackman for very competent technical assistance in the determination of some of the spectral data. They also wish to thank the Fisheries Research Board of Canada for financial support, since the major part of this work was carried out under a contract between the Fisheries Research Board of Canada and Memorial University of Newfoundland. The authors further acknowledge the general assistance of the National Research Council in support of these studies.

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LIGHT ABSORPTION STUDIES

PART XV. THE ULTRAVIOLET ABSORPTION SPECTRA OF ANISOLES[1]

J. C. Dearden and W. F. Forbes

ABSTRACT

Anisoles, compared with phenols, possess similar spectral properties, except that properties determined mainly by the hydrogen atom of the hydroxy group are modified. In this way, comparison of the ultraviolet absorption spectra of phenols and anisoles permits, for example, the study of the spectral effects of hydrogen bonding and the study of steric interactions involving the hydroxy and methoxy groups.

INTRODUCTION

In previous parts of this series (1) it was found that ultraviolet *B*-band spectra can often be interpreted by assuming that the *B*-bands of ultraviolet spectra are determined predominantly by mesomeric and steric interactions. Phenolic spectra, which were examined in the previous paper (1*a*), were found to be of interest since they provide good examples of secondary interactions such as intramolecular hydrogen bonding. The phenolic *B*-band is also of interest, since it is believed to be determined by so-called locally excited states; that is, in the absence of appreciable direct mesomeric interaction between the hydroxy group and the benzene ring, the benzene ring is assumed to determine the observed absorption band with the hydroxy group exerting only a secondary influence. The anisole spectra provide an evident extension of this investigation, and we have therefore determined, or redetermined, a number of the relevant anisole spectra.

THE SPECTRUM OF ANISOLE

Table I lists the main absorption maxima of anisole in the region 210–330 mμ.

Anisole in cyclohexane absorbs maximally at 220 mμ, that is, at longer wavelength than the corresponding absorption of phenol at 210 mμ (1*a*). We deduce from this that the methoxy group does not merely exert a "secondary" interaction on the benzene ring, as has been postulated for the spectrum of phenol, since such a secondary interaction would cause a wavelength displacement of only *ca.* 7 mμ relative to benzene (see ref. 1*a* and section on metasubstituted anisoles). This in turn suggests that some additional mesomeric interaction occurs between the methoxy group and the benzene ring or, in other words, that the transitions leading to the *B*-band in anisole involve a smaller proportion of locally excited states compared with the transitions leading to the *B*-band in phenol.

The important question arises why locally excited states should preferentially contribute to this absorption in phenol. One possible explanation is that in phenol the O—H bond is aligned approximately parallel to the plane of the benzene ring (I*a*), whereas in anisole, partly for steric reasons, the O—CH_3 bond is directed out of the plane of the benzene ring as in I*b*. To satisfy this explanation, it must further be assumed that this direction of the O—CH_3 bond as in I*b* favors the overlap of the unshared electrons of the oxygen atom with the π-electrons of the benzene ring, and that in this way additional resonance interaction is possible. This explanation is consistent with the observation that the spectrum of phenol in ether or ethanol solution, which presumably involves the attachment of a solvent molecule to the phenolic hydrogen atom and hence causes an

[1]*Manuscript received February 12, 1959.*
Contribution from the Memorial University of Newfoundland, St. John's, Newfoundland.

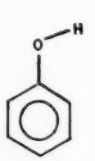
TABLE I

Absorption maxima of anisole in various solvents*

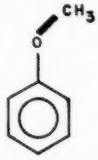
Solvent	*B*-Band		*C*-Band	
	λ_{max} (mμ)	ϵ_{max}	λ_{max} (mμ)	ϵ_{max}
Vapor	214	†	*ca. 254* *ca. 259* 261 266 267 272.5	†
Cyclohexane‡	220 *ca. 223*	7500 *6000*	263 269 275	1400 2100 2100
Ether	219	7400	263.5 269 275.5	1300 1900 1700
Ethanol	219	7000	264 269 275	1350 1800 1600
Water	217	4300	*ca. 261* 267 273	*1200* 1600 1300
0.1 *N* HCl	217	4900	267 272	1700 1400
N NaOH	221	3600	267 273	1700 1400
Conc. H_2SO_4	235–236	11300	281	1350

*Values in italics represent inflections in this and subsequent tables.
†Intensities not determined.
‡Solute concentration = 2.3×10^{-4} moles/l.

increase in the effective size of the hydroxy group, shows maximal absorption at or near 218 mμ (1*a*), namely much like that of anisole in most solvents (see Table I). This therefore may imply that under these conditions structures such as I*a*, partly for steric reasons, tend to change into structures of type I*b* which facilitate orbital overlap and which tend to give rise to a maximal absorption near 218 mμ.*



I*a*



I*b*

The *C*-band fine structure, which is observed in cyclohexane solution for the spectra of both anisole and phenol, is evident, though to a lesser extent, for anisole in aqueous and alcoholic solution. It almost disappears for phenol in the latter solvents (1*a*). This reduced fine structure in the *C*-bands of both anisoles and phenols is ascribed to solute–solvent interactions (cf. ref. 1*a*). A striking difference between the spectra of phenol and anisole is the different behavior of both *B*- and *C*-band maxima on changing the

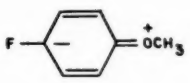
*For a full discussion concerning the conformation of the methoxy group, with particular emphasis on the tendency of the methoxy group to be coplanar with the benzene ring, see Wheland, G. W. Resonance in organic chemistry. John Wiley & Sons, Inc., New York. 1955. pp. 238–243.

solvent from neutral to basic; the phenolic bands are appreciably displaced to longer wavelength (1*a*), while addition of alkali to an aqueous solution of anisole only slightly displaces the *B*-band (by 4 mμ), and does not displace the *C*-band (see Table I).

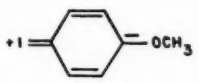
THE SPECTRA OF PARASUBSTITUTED ANISOLES

As in previous parts (1), the spectra of paradisubstituted benzene derivatives may be classified into spectra of compounds when both substituents are electron-donating, or electron-withdrawing, and into spectra of compounds when one substituent is electron-donating and the other electron-withdrawing. For the former group, the spectrum of the disubstituted benzene compound usually resembles the spectrum of the monosubstituted parent compound, that is, the transition involves locally excited states with the second substituent exerting only a secondary influence on the spectrum. If in the former group, in addition, the two substituents are dissimilar, the spectrum of the monosubstituted compound will involve the substituent which interacts preferentially with the benzene ring. These generalizations are illustrated by the data in Table II.

The earlier *B*-band spectra of parasubstituted anisoles listed in Table II usually show the anisole-type spectrum. Exceptions are provided when the methoxy substituent does not preferentially interact with the benzene ring. For example, for *p*-aminoanisole, and incidentally for the meta and ortho isomers also, in non-acidic media an aniline-type *B*-band is obtained, and for *p*-iodoanisole an iodobenzene-type spectrum is obtained. This may be illustrated by assuming structures of type II or III to be involved preferentially in the transitions leading to the spectra of *p*-fluoro- and *p*-iodo-anisole.*



II



III

If the parasubstituent is electron-withdrawing (see lower part of Table II) the anticipated appreciable wavelength displacements, accompanied by intensity increases, are observed in the *B*-band. These wavelength displacements are shown in Fig. 1 to be parallel to the wavelength displacements obtained for phenols. The electron-withdrawing substituent may be visualized as facilitating the formation of resonance forms of type IV.

**The second substituent will in this way exert only a secondary effect on the B-band. Thus the location of the B-band remains essentially unaltered between p-fluoroanisole and anisole. Fluorobenzene, by contrast, shows the following, quite different, B-band absorption in cyclohexane solution, that is, λ_{max} 204 mμ, ε = 6600. Iodobenzene, on the other hand, shows a B-band reasonably similar to that of p-iodoanisole, that is: λ_{infl} 223 mμ, ε = 9400; λ_{max} 227 mμ, ε = 12,700; and λ_{max} 232 mμ, ε = 12,000 (see also Table II). Moreover, the bathochromic B-band wavelength displacements reported by Schubert et al. (3) on determining the B-bands in the vapor phase and in cyclohexane solution are 2.8 and 4.6 mμ for p-fluoroanisole and anisole respectively, while there is a hypsochromic wavelength displacement of 2 mμ for fluorobenzene. Therefore in only one of the two examples will the "second" substituent be a halogen atom, and it follows from this that care must be taken in deducing the order of electron release for the halogen atoms from the spectra of para-halogen-substituted anisoles (cf. refs. 3, 4).*

It may also be noted that the C-band spectral changes do not entirely bear out this analysis, since the C-band changes suggest a different pattern for p-fluoroanisole and the other three para-halogen-substituted anisoles. However, although we are not strictly concerned with C-band changes at this time, it may be observed that the location of the C-band maxima are closer to the location of the C-band maxima in anisole than to the location of these maxima in fluorobenzene (λ_{max} 246.5 mμ, ε = 350; λ_{max} 252 mμ, ε = 750; λ_{max} 258 mμ, ε = 1100; and λ_{max} 264 mμ, ε = 1050), and the C-band fine structure in p-fluoroanisole is also obtained for para-alkyl-substituted anisoles and cannot therefore be associated specifically with the fluoro substituent. In addition, the iodobenzene C-band fine structure (λ_{infl} 246 mμ, ε = 590; λ_{max} 251 mμ, ε = 670; λ_{max} 255.5 mμ, ε = 710; and λ_{max} 261 mμ, ε = 620) is similar to that in p-iodoanisole (see Table II).

TABLE II

Absorption maxima of substituted anisoles in cyclohexane solution

	Para isomer				Meta isomer						Ortho isomer					
	B-Band		*C*-Band		Anisole *B*-band		2nd *B*-band		*C*-Band		Anisole *B*-band		2nd *B*-band		*C*-Band	
Substituent	λ_{max} (mμ)	ϵ_{max}	λ_{max} (mμ)	ϵ_{max}	λ_{max} (mμ)	ϵ_{max}	λ_{max} (mμ)	ϵ_{max}	λ_{max} (mμ)	ϵ_{max}	λ_{max} (mμ)	ϵ_{max}	λ_{max} (mμ)	ϵ_{max}	λ_{max} (mμ)	ϵ_{max}
-OCH_3	210–211	5700*	*ca. 280*	*2500*	220	7300	—	—	*ca. 267*	*1700*	225	7150	—	—	271	2450
	226	9700	286.5	3200					271.5	2200					275	2550
			290	3200					277.5	2150					280	1900
			297	2550												
-OH	223–224	7000	*ca. 285*	2900	220	5400			*ca. 267*	*1300*	216	6200			*ca. 270*	*2250*
			288	3150					271.5	1700					273.5	2550
			291	3100					278	1550					279.5	2150
			298	2350												
-NH_2	236	9100	300	2600			233–234	6400	283	2250			237	8500	286	3450
			303	2650					*ca. 289*	*1800*						
-NH_2†	230	7900	293	2000			229	6400	279	2000			231	6900	278	2650
															280	2700
-NH_2‡	219.5	8250	269.5	1450	218.5	7700			267.5	1800	215.5	6800			267	1950
			ca. 275	*1200*					*ca. 273*	*1550*					273	1700
-CH_3	222.5	8600	268	1450	217	7000			*ca. 266*	*1300*	215.5	7500			270	2000
			271	1600	*ca. 220*	*6800*			270.5	1800	*ca. 220*	*7100*			276	1900
			274	1900					277.2	1900						
			276.5	2200												
			283	2050												
-F	*ca. 211*	*5000**	*ca. 267*	*1650*	218	7500			*ca. 263*	*1250*	217.5	7100			264.5	1450
	216–217	5400	269.5	2150					266.5	1550					268	1700
			272.5	2500					272.5	1450					273	1450
			275	2750												
			278.5	3200												
			284.5	2750												

TABLE II (*Concluded*)

Absorption maxima of substituted anisoles in cyclohexane solution

	Para isomer				Meta isomer						Ortho isomer					
	B-Band		*C*-Band		Anisole *B*-band		2nd *B*-band		*C*-Band		Anisole *B*-band		2nd *B*-band		*C*-Band	
Substituent	λ_{max} (mμ)	ϵ_{max}	λ_{max} (mμ)	ϵ_{max}	λ_{max} (mμ)	ϵ_{max}	λ_{max} (mμ)	ϵ_{max}	λ_{max} (mμ)	ϵ_{max}	λ_{max} (mμ)	ϵ_{max}	λ_{max} (mμ)	ϵ_{max}	λ_{max} (mμ)	ϵ_{max}
-Cl	227	11700	*ca. 278*	*1400*	219	7300			*ca. 266*	*1350*	218	7500			*ca. 267*	*1600*
			279	1900					272	2150	222	7400			272.5	2400
			287	1850					279	2150					280	2450
-Br	226	12500	*ca. 274*	*1350*	*ca. 218*	*8500*			*ca. 267*	*1450*	*ca. 218*	*8300*			*ca. 268*	*1800*
			279	1750					272.5	2350	*ca. 223*	*7400*			273.5	2750
			287	1550					279.5	2300					280.5	2800
-I	233	19000	273.5	1450	213	25500*	*ca. 224*	*9200**	268	1950			*ca. 227*	*8700**	269	2400
	ca. 237	*15800*	279	1600			228.5	9500	274.5	2700			231	10200*	275.5	3400
			288	1200					282	2550			235.5	10000*	283	3250
$-COCH_3$	261.5	18000	—	—	214	25000*	244	8500	298	2800	211	20300*	*ca. 237*	*8100*	294.5	3550
	ca. 268	*14500*					*ca. 250*	*6100*	*ca. 308*	*2100*			241	8350	*ca. 304*	*2500*
	ca. 273	*11200*														
-CHO§	265	18500	—	—	216	23500	246	9200‖	304	3000	211	20000*	246	10500	306	4600
	ca. 272	*16000*			220	22500	*ca. 251*	*8900*‖	*ca. 313*	*2700*			*ca. 253*	*8500*	*ca. 314*	*4200*
	278	12500														
	286	5500														
$-NO_2$	291	12100	—	—	223	13000	260	6100	313	2400	—	—	248–249	3400	304	2500
$-NO_2$†	313	10500	—	—	228	8900	273.5	6000	330	2050¶	*ca. 232*	*4300*	264	4300	333	2900
-COOH	255	17300	—	—	211	26000*	238	8500	295	3200			229	8000	282	2950
	ca. 263	*13500*							*ca. 301*	*2900*			*ca. 256*	*5000*	*ca. 286*	*2750*
	ca. 269	*9000*													289	2750

*B-Band assignment doubtful. †In aqueous solution. ‡In 0.1 *N* HCl. §In *n*-hexane solution. ‖These values should replace those previously reported (see ref. 1*c*). ¶Ref. 2.

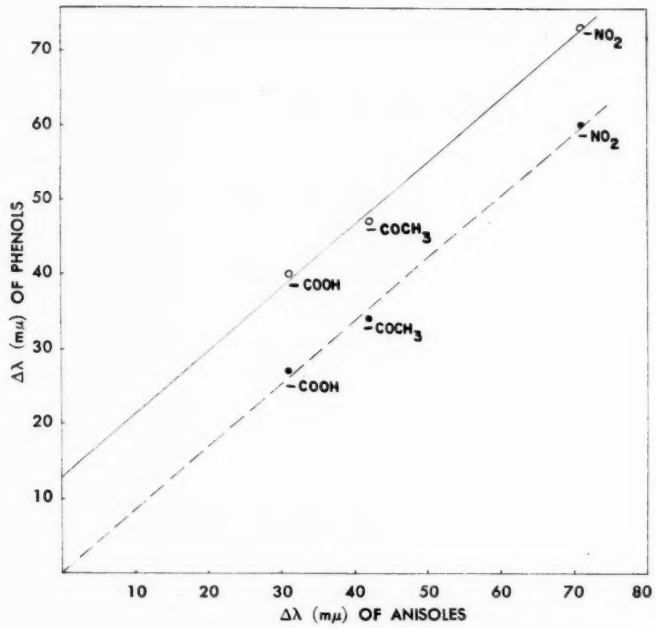
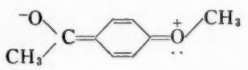
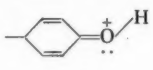


FIG. 1. Wavelength displacements ($\Delta\lambda$) of the *B*-band obtained in neutral inert solution on introducing an electron-withdrawing parasubstituent in anisole and phenol. (Values from this study, and ref. 1*a*.) The dotted line shows the plot if the phenolic absorption at 223 mμ is used as the reference compound (see text). ○ $\Delta\lambda$ for phenols taken as (λ_{max} −210). ● $\Delta\lambda$ for phenols taken as (λ_{max} −223).

The appreciable wavelength displacements for parasubstituted phenols are calculated with reference to a hypothetical absorbing species absorbing maximally at 223 mμ, and



IV



V

involving in its transitions structures of type V to an appreciable extent. If, on the other hand, the phenolic absorption in cyclohexane at 210 mμ is assumed to involve preferentially electronic excited states of type V and is taken as the reference point, then the straight line, as shown in Fig. 1, does not pass through the origin. The data thus lend support to the suggestion made in the previous paper concerning the supposed absence of appreciable mesomeric interaction for phenol in cyclohexane solution (see section on the spectrum of anisole and ref. 1*a*).

The *C*-bands of para- and meta-substituted anisoles undergo the previously noted general changes (1*e*). Moreover, the *C*-band spectral changes are similar for para- and meta-substituted phenols and anisoles (see previous paper).

THE SPECTRA OF METASUBSTITUTED ANISOLES

The *B*-bands of meta- and ortho-substituted anisoles are again classified into *B*-bands associated with the anisole chromophore, and into *B*-bands associated with the other

monosubstituted benzene chromophore (cf. refs. 1*a*, *b*, *c*, *d*). The two types of *B*-bands are in this way observed in a number of meta- and ortho-substituted anisoles.*

Using this classification, it may first be noted that the "secondary effect" of the methoxy group on the *B*-band associated with the non-anisole, monosubstituted benzene chromophoric system is as anticipated. That is, the non-anisole *B*-bands are generally bathochromically displaced by *ca.* 7 mμ for compounds where the second substituent is electron-withdrawing (see Table II and cf. ref. 6), and it is thus assumed that the overall effect of the methoxy group facilitates the formation of electronic excited states.

The effect of the second substituent on the anisole *B*-band is very similar to the effect of the same substituent on the phenolic *B*-band. Both the phenol and anisole *B*-bands are frequently displaced to longer wavelength if the second substituent is electron-withdrawing, and the displaced *B*-bands are sometimes more intense than for the parent compounds, namely phenol or anisole. For compounds of this type the observed intensities of the *B*-bands also suggest that the anisole *B*-band absorption occurs preferentially (see Table II). This again supports the previously noted generalization that, in the absence of direct primary resonance interaction, an electron-withdrawing substituent tends to cause an intensity increase (see refs. 1*a*, 1*d*, 7).

THE SPECTRA OF ORTHOSUBSTITUTED ANISOLES

Comparing the *B*-bands of orthosubstituted phenols and anisoles it is found that frequently only the *B*-band of the phenol is appreciably intensified and displaced to longer wavelength. Other secondary interactions may evidently contribute to these observed spectral changes but the data certainly provide qualitative evidence for intramolecular hydrogen bonding, since the above-mentioned spectral changes are most pronounced if a strong intramolecular hydrogen bond is expected. Qualitative evidence for intramolecular hydrogen bonding may also be obtained by comparing the spectra of ortho isomers with those of the meta isomers; for intramolecularly hydrogen-bonded phenols the bathochromic wavelength displacement and intensity increase in both *B*- and *C*-bands are greater between the ortho- and meta-substituted phenols than between the corresponding anisoles. A fuller discussion of semiquantitative methods, which may be used to estimate the strength of the intramolecular hydrogen bond in orthosubstituted phenols and related compounds, will be presented in a separate communication.

Steric effects have, by implication, been noted in the section on the spectrum of anisole since it has been tentatively assumed that, partly for steric reasons, the methoxy group in anisole is directed out of the plane of the benzene ring. It follows that an orthosubstituent would not be expected readily to cause an appreciable wavelength displacement or intensity decrease, since the methoxy group is already dislodged from the plane of the benzene ring. In fact, even for bulky orthosubstituents, the maximal *B*-band absorption still occurs close to 220 mμ (see Table III). It should be noted, however, that for compounds such as 2,6-dimethylanisole or *tert*-butoxybenzene appreciable spectral changes can be discerned in the *C*-band (see Table III and ref. 8). For example, the *C*-band of 2,6-dimethylanisole as shown in Table III is considerably less intense than the *C*-band

**Only one B-band is usually observed for the para isomer, although a band that may, incorrectly, be assumed to be a second B-band occurs in compounds like p-nitroanisole at λ_{max} 227 mμ, ε = 7000 (in water). However, this absorption band, which also occurs in p-nitrophenol at λ_{max} 227 mμ, ε = 7000 (in water), is not a B-band, since in basic solution this band of p-nitrophenol still occurs at λ_{max} 226 mμ, ε = 6500 (in N* NaOH) *(5). If the absorption band were a B-band, addition of alkali would appreciably displace the band to longer wavelength (1a) and because this is not so, the absorption bands near 227 mμ in p-nitrophenol and p-nitroanisole are both assumed to be A-bands.*

in 3,5-dimethylanisole. The latter compound in cyclohexane solution absorbs as follows: λ_{max} 219–220 mμ, ϵ = 7250 (*B*-band); λ_{infl} *ca.* 264 mμ, ϵ = 900; λ_{infl} *ca.* 268 mμ, ϵ = 1250; λ_{max} 271 mμ, ϵ = 1450; λ_{infl} *ca.* 274 mμ, ϵ = 1250; and λ_{max} 278 mμ, ϵ = 1700. 2,5-Dimethylanisole also absorbs similarly, thus: λ_{max} 219 mμ, ϵ = 7200 (*B*-band); λ_{infl} *ca.* 266 mμ, ϵ = 1400; λ_{infl} *ca.* 270 mμ, ϵ = 1900; λ_{max} 273 mμ, ϵ = 2100; and λ_{max} 278.5 mμ, ϵ = 2150.

TABLE III

Absorption maxima of orthosubstituted anisoles in cyclohexane and ethanol

	Cyclohexane				Ethanol			
	B-Band		*C*-Band		*B*-Band		*C*-Band	
Orthosubstituents	λ_{max} (mμ)	ϵ_{max}	λ_{max} (mμ)	ϵ_{max}	λ_{max} (mμ)	ϵ_{max}	λ_{max} (mμ)	ϵ_{max}
H,H	220	7500	263	1400	219	7000	264	1350
	ca. 223	*6000*	269	2100			269	1800
			275	2100			275	1600
H,CH_3	215.5	7500	270	2000	215.5	6800	269	1850
	ca. 220	*7100*	276	1900	*ca. 219*	*6700*	275	1750
H,$CH(CH_3)_2$	216	7200	*ca. 263*	*1450*	216.5	7100	*ca. 263*	*1450*
	220	7100	269	2100	*ca. 220*	*7000*	269	2050
			275.5	2000			275	1900
H,$C(CH_3)_3$	216.5	7200	*ca. 262*	*1350*	*ca. 217*	*7000*	*ca. 262*	*1400*
	221	7300	268	2000	221	7200	268	2000
			274.5	2000			274.5	1900
CH_3,CH_3	212	8350	262.5	345	*ca. 211*	*8350*	262	315
			266	340			266	310
			270.5	300			270	260
$CH(CH_3)_2$,$CH(CH_3)_2$	212	9400	263	400	*ca. 211*	*9200*	263	380
			ca. 265	*385*			*ca. 265*	*365*
			270	360			269.5	335

Table III lists the spectra of some orthosubstituted anisoles. The data show that changing the solvent from cyclohexane to ethanol has practically no effect on the observed *B*- and *C*-bands of many of these compounds. This absence of solvent effect has previously been noted for orthosubstituted phenols. Both phenol and anisole data are therefore consistent with the explanation put forward in the previous paper, that a large orthosubstituent prevents solvent–solute interaction between the unshared electron pair of the oxygen atom and the ethanol molecules.

The frequent similarity of the spectra of the ortho and meta isomers, which has been observed for phenols (1*a*), is also observed for the anisole analogues. However, there are some significant differences. Thus, the intensity decreases which may be caused partly by steric interactions are frequently more pronounced for anisoles. For example, comparing the nitrobenzene *B*-bands of the meta and ortho isomers of nitrophenol and nitroanisole, it is found that the decrease of the ϵ_{max} values in the ortho isomers is more pronounced for *o*-nitroanisole. Unfortunately, this example does not lend itself to unambiguous analysis since in neutral solution intramolecular hydrogen bonding affects the *B*-band of *o*-nitrophenol, while in basic solution the effective size of the methoxy group is compared with that of the O^- group rather than with the effective size of the hydroxy group. However, it seems certain that a steric factor contributes to the relatively low ϵ_{max} value of *o*-nitroanisole in various solvents (see Table II). Supporting evidence for the

ability of the methoxy group to cause steric inhibition of resonance is further provided by the spectrum of 2,6-dimethoxynitrobenzene in cyclohexane solution (λ_{max} 276 mμ, ϵ = 1700) which shows a yet more pronounced decrease in intensity for the nitrobenzene *B*-band. Further, for ortho-halogen-substituted phenols and anisoles, the ϵ_{max} values of the ortho-fluoro and ortho-chloro compounds are *smaller* for the phenols than for the anisoles, but for the ortho-bromo compound, that is, for a larger orthosubstituent, the ϵ_{max} value of the orthosubstituted phenol is *greater* than that of the anisole (see Table II and ref. 1*a* for the relevant *B*-bands; for evidence of steric interactions because of the methoxy group, see also refs. 9, 10).

In orthosubstituted anisoles there is also evidence that large steric interactions contribute to more pronounced spectral changes. For example, in 2,6-dimethylanisole a hypsochromic wavelength displacement, indicative of steric interaction, is obtained in the *B*-band, and the *C*-band is very considerably reduced in intensity (see Table III). It may finally be noted that in many hindered phenols and anisoles, that is, in compounds where *C*-band fine structure is evident in both cyclohexane and ethanol solutions, a relative decrease in intensity occurs for the long wavelength peak of the *C*-band in ethanol solution (see, for example, in Table III the *C*-bands of *o-tert*-butylanisole in cyclohexane and ethanol solution).

EXPERIMENTAL

The ultraviolet absorption spectra were determined by standard methods using Unicam SP 500 spectrophotometers. For each compound at least two independent sets of observations were made. Some of the spectra have previously been described in this series and elsewhere. Whenever possible, the anisole spectra were determined under conditions identical with those under which the phenolic spectra had been determined. Frequently, but not always, our data were in good agreement with recent values reported by other workers (cf. refs. 4, 5, 11, 12, 13).

The anisoles were mostly commercial materials, purified by distillation or recrystallization until their boiling points or melting points showed them to be sufficiently pure. The solvents used were spectroanalyzed cyclohexane (Fisher) or commercially available absolute ethanol.

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PHOTOCHEMICAL SEPARATION OF MERCURY ISOTOPES

IV. THE REACTION OF $Hg^{202}6(^3P_1)$ ATOMS, PHOTOEXCITED IN NATURAL MERCURY VAPOR, WITH METHYL CHLORIDE AND ISOPROPYL CHLORIDE[1, 2]

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ABSTRACT

A detailed investigation has been made of the reaction of $Hg^{202}6(^3P_1)$ atoms, photoexcited in natural mercury vapor (Hg^N), with methyl chloride, at room temperature. Data are also reported on the reaction with isopropyl chloride as substrate. Hg^{202} enrichment in the calomel product is taken as evidence of its formation in the primary quenching reaction.

Under static conditions the methyl chloride reaction was found to form calomel with the natural Hg^{202} abundance (29.8%). With increasing flow rate a progressive increase in Hg^{202} abundance was observed. Maximum enrichments were found at fast flow rates, low substrate pressures, and high values for the absorbed light intensity (I_A). The most highly enriched calomel obtained in this study contained 50.4% Hg^{202}. With increasing I_A, a corresponding increase in flow rate was required to achieve maximum Hg^{202} enrichment. The addition of propylene or butene-1 to the methyl chloride stream was found to result in a slight decrease in Hg^{202} abundance over that for the pure substrate.

The isotopically specific aspects of the reaction are explained in terms of the sequence:

$$RCl + Hg^{202}6(^3P_1) \rightarrow Hg^{202}Cl + R \qquad [1]$$

$$RCl + Hg^{202}6(^3P_1) \rightarrow R + Cl + Hg^{202}6(^1S_0) \qquad [2]$$

$$Cl + Hg^N + M \rightarrow Hg^NCl + M \qquad [3]$$

where M represents a third body, including the wall. The decrease in enrichment observed at high substrate pressures is shown to be due to Lorentz-broadening effects on the hyperfine absorption contours of Hg^N. The failure to obtain enrichment under static conditions is explained by the depletion in Hg^{202} of the Hg^N in the cell through reaction [1].

The investigation shows that there are two primary processes operative in the mercury-$6(^3P_1)$-photosensitized decomposition of alkyl chlorides, in one of which calomel is formed. These processes presumably involve a common short-lived intermediate R—Cl—Hg.

INTRODUCTION

In the investigation reported in this paper, the technique of mono-isotopic mercury-$6(^3P_1)$-photosensitization, in natural mercury vapor (Hg^N), developed in a previous study in this series (1), has been used to study the reaction of $Hg^{202}6(^3P_1)$ atoms, in Hg^N, with two alkyl chlorides. The effect of reaction parameters on the Hg^{202} content of the calomel product of the methyl chloride reaction has been investigated in some detail. Preliminary experiments with isopropyl chloride as substrate are also given for comparative purposes. As in the earlier investigation with hydrogen chloride (2), Hg^{202} enrichment in the calomel product is taken as evidence of formation of the product in the primary quenching process.

In an investigation of the reaction of flowing hydrogen chloride with $Hg^{202}6(^3P_1)$ atoms in Hg^N, McDonald, McDowell, and Gunning (2) found that the calomel product contained a maximum of 44% Hg^{202}, under conditions of fast flow and low substrate pressure. This Hg^{202} abundance corresponds to an enrichment of 48% over the natural Hg^{202} abundance of 29.8%. In the presence of unsaturated addends, such as butadiene-1,3, the Hg^{202} enrichment was found to increase to a maximum of 98%.

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The $Hg^N6(^3P_1)$-photosensitized decomposition of methyl chloride has been investigated by Masson and Steacie (3) over the pressure range 10–640 mm at temperatures from 72 to 328° C. These authors concluded that the calomel product, under the afore-mentioned conditions, arises from the secondary reaction of unexcited Hg^N with CH_2Cl radicals. By photosensitization of a single isotopic species, as in the present study, fairly unequivocal evidence can be obtained on the importance of primary formation of mercury compounds in alkyl chloride reactions. The present investigation was undertaken, therefore, to gain further insight into the nature of the primary process in the mercury-$6(^3P_1)$-photosensitized decomposition of calomel-forming substrates.

EXPERIMENTAL

The high-vacuum flow system was so arranged that reproducible gas flow rates could be achieved for compounds which were either gases (CH_3Cl) or liquids ($(CH_3)_2CHCl$) at room temperature. The pressure of the flowing gas was measured with a manometer upstream from the reaction cell. Flow rates were determined by calibrated capillary flow meters situated on the entrance and exit sides of the reaction cell.

The methyl chloride was taken directly from a cylinder. To obtain a fixed pressure of isopropyl chloride vapor, the temperature of the liquid was held constant in a modified Ward still (4). The flow rate was controlled with a Warrick–Fugassi valve (5). Efficient saturation of the gases with Hg^N was accomplished by allowing the gases to pass through an operating "umbrella-type" mercury diffusion pump. The exit condenser of the pump was temperature-regulated to $\pm 0.5°$ C by circulating water from a thermostat through its jacket.

The reaction cells used were rectangular in shape, with faces 2.5 cm × 8.0 cm and an internal path length of 0.1 cm. They were made of Vycor 7910 glass, and attached to the system by offset arms, terminating in 12/5 spherical joints.

The Hg^{202} source and photometric apparatus have been previously described (2). The reaction cell was located 5 cm from the source. A rectangular slit was used to confine the beam within the cell faces. A portion of the transmitted radiation was focussed on a Westinghouse WL-775 photocell by means of a quartz lens.

A special procedure was employed in the determination of the relative mean absorbed light intensity during a run. The relative intensity of the source could be obtained at any time by rotating the cell through 90° out of the light path. Before attaching the cell to the system, the transmission of the cleaned, Hg^N-free, cell was first measured in the absorbiometric analysis apparatus (6). With the cell in position, and the Hg^N-saturated gas flowing through the system, the transmission was again measured. From these data, together with the calibration curve obtained on the analysis system (6), the fraction of light absorbed by the Hg^N in the cell, and the Hg^N concentration, could be calculated. During the reaction, the determination of absorbed intensity was complicated by the accumulation of the calomel product on the faces of the reaction cell. Preliminary experiments showed that the transmitted intensity was reduced by calomel deposition to approximately one-half of the initial value in the first 5–10 minutes of irradiation. At this half-time point, the cell was rotated out of the light beam, and the faces were heated with a Bunsen burner until the calomel had sublimed away. After it was cooled, the cell was again moved into the light beam. It was consistently observed in this procedure that subsequent calomel deposition occurred largely in the area to which the original calomel product had been sublimed. Thus the transmitted intensity did not decrease as rapidly in the latter part of the run, as in the initial period. Usually

the transmitted intensity was again reduced to one-half after 30 to 60 minutes of further irradiation. The run was terminated at this point by rotating the cell out of the light path. The method of recovering the isotopic mercury from the calomel, and the procedure for isotopic analysis, have been previously described (1, 6). Before the reaction cell was used again, it was cleaned with hot aqua regia, rinsed, and dried at 120° C. In order to obtain reproducible enrichment data, it was found necessary, also, to heat the cell to a dull red heat prior to each run.

The methyl chloride, propylene, and butene-1 used were Matheson C.P. grade, with minimum purity of 99%. The isopropyl chloride used had a boiling range of 34–36° C. It was purified by several trap-to-trap distillations before use.

RESULTS

A preliminary series of runs was first made on the methyl chloride reaction. The Hg^{202} abundance in the calomel product was studied as a function of flow rate, at a fixed pressure of 7 mm. The incident intensity, I_0, was maintained essentially constant in this series. It should be noted that throughout this paper intensity will be expressed in terms of scale divisions on the 5×10^{-10} ampere scale of the Beckmann Ultrohmeter, used for monitoring the photocell output (6). Since the relative positions of all optical components were held constant in this investigation, the intensity values given are directly proportional to the absolute intensities.

The data are presented in Table I, and shown graphically in Fig. 1. It will be noted that two "saturation temperatures" were used. By this term is meant the temperature of the water circulating through the exit arm of the mercury saturator. From Fig. 1, it can be seen that the Hg^{202} abundance increases directly with the flow rate. With the saturator temperature at 9° C the abundance appears to maximize at 42.7% Hg^{202}. Considerably higher abundances were found with the saturator temperature at 20° C. At a flow rate of 22.5 liter minute^{-1}, an abundance of 50.4% Hg^{202} was obtained at the higher saturator temperature. It should also be pointed out, at this time, that no enrichment was found under static conditions. In Fig. 1, it can be seen that the Hg^{202} abundance approaches the natural value of 29.8% as the flow rate goes to zero.

Under the conditions of constant I_0, saturator temperature, and substrate pressure obtaining in the first series, variations were observed in the intensity absorbed by the

TABLE I

The effect of flow rate on the Hg^{202} content of the solid product of the reaction of $Hg^{202}6(^3P_1)$ atoms, photoexcited in Hg^N, with methyl chloride

Pressure, mm	Saturation temperature, ° C	Flow rate, liter min^{-1}	Incident intensity, I_0	Hg^{202} abundance, atom %
7.00	20.5	0.18	0.67	31.0
7.00	20.5	0.26	0.68	34.3
6.73	20.5	0.41	0.64	38.4
7.06	20.0	0.90	0.68	38.7
6.60	18.5	3.88	0.69	41.8
7.62	20.5	11.0	0.65	46.0
6.64	20.5	22.5	0.65	50.4
7.06	9.5	0.46	0.65	33.8
6.62	8.2	5.34	0.64	42.8
6.45	9.0	9.70	0.63	42.6

mercury vapor. In subsequent runs, therefore, the effect of this parameter was studied in some detail.

To evaluate the intensity, I_A, absorbed by the mercury in the reaction cell, the ratio of transmitted to incident intensity was determined for the evacuated cell ($\bar{T}_C$) and also for the cell under reaction conditions ($\bar{T}_R$). The two faces of the cell were assumed to be identical, and the fraction of light transmitted by the incident face, by the filter-product rule, was taken as the square root of $\bar{T}_C$. With I_0 as the mean incident intensity of the lamp during the reaction, I_A was calculated from the equation

$$I_A = \bar{T}_C^{\frac{1}{2}}(1-\bar{T}_R/\bar{T}_C)I_0 = \bar{T}_C^{\frac{1}{2}}.A.I_0.$$

Values of A were determined at the beginning of the run, and also following sublimation of the calomel at the half-time point, in most of the runs.

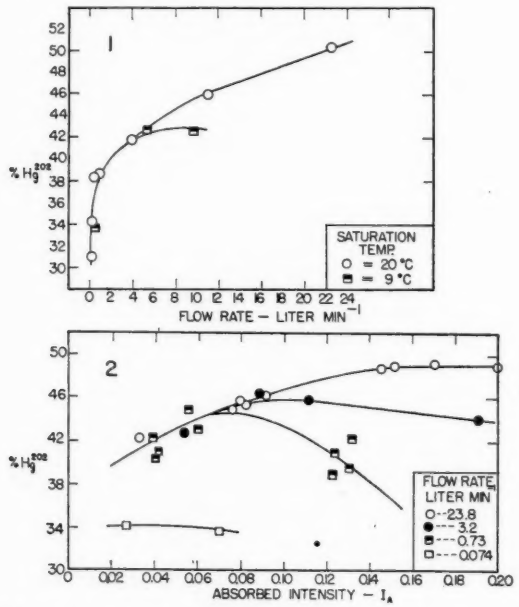

FIG. 1. The effect of flow rate on the abundance of Hg^{202} in the calomel product of the methyl chloride reaction, at two saturation temperatures.

FIG. 2. The effect of I_A on the abundance of Hg^{202} in the calomel product of the methyl chloride reaction, at four flow rates.

In Table II, the Hg^{202} abundance is shown as a function of I_A, for mean flow rates of 0.074, 0.73, 3.2, and 23.8 liter minute^{-1}. In the graphical representation of the data in Fig. 2 it would appear that the Hg^{202} abundance passes through a maximum then decreases with increasing absorbed intensity, except at the highest flow rate used, i.e. 23.8 liter minute^{-1}. In other words, for each absorbed intensity there is a minimum value of the flow rate which must be achieved in order to obtain maximum isotopic enrichment. These minimal flow rate values increase with increasing absorbed intensity. With the flow rate sufficiently high to eliminate any enrichment-depressing effect of this parameter, the Hg^{202} abundance clearly increases with increasing absorbed intensity.

TABLE II

The effect of flow rate and absorbed intensity on the Hg^{202} content of the solid product of the reaction of $Hg^{202}6(^3P_1)$ atoms, photoexcited in Hg^N, with methyl chloride

	Pressure, mm	Flow rate, liter min^{-1}	Saturation temperature, °C	Absorption (A) Initial	Absorption (A) Half-time	I_0	I_A	Hg^{202} abundance, atom %
	7.86	25	20.0	0.320		0.146	0.033	42.3
	7.14	25.4	20.5	0.346		0.305	0.076	44.9
	7.00	18.2	29.6	0.385		0.655	0.080	45.8
	6.76	21.0	30.5	0.364	0.377	0.710	0.083	45.4
	6.94	23.1	21.0	0.264		0.496	0.092	46.2
	6.59	25.7	20.5	0.389	0.410	0.527	0.146	48.8
	7.21	25.8	20.5	0.333		0.645	0.152	49.0
	6.45	25.2	19.5	0.338	0.408	0.580	0.171	49.2
	6.80	23.5	21.0	0.402	0.394	0.700	0.200	48.9
	6.86	27.2	30.6	0.436	0.410	0.655	0.204	50.2
	6.58	21.2	30.7	0.428	0.444	0.590	0.206	49.8
Average values	6.9	23.8						
	7.13	3.94	20.5	0.484	0.468	0.360	0.054	42.8
	6.96	3.13	21	0.489	0.500	0.570	0.089	46.4
	7.69	2.77	20.5	0.425	0.378	0.885	0.112	45.9
	6.87	3.22	20.5	0.402	0.522	0.560	0.191	44.0
Average values	7.2	3.2						
	6.80	0.73	21.2	0.291	0.328	0.178	0.039	42.2
	6.8	0.7	31.5	0.303	0.312	0.192	0.041	40.4
	6.46	0.78	20.5	0.180	0.276	0.270	0.042	41.1
	6.80	0.76	21.0	0.164	0.225	0.418	0.056	44.8
	6.80	0.76	21.2	0.232	0.292	0.325	0.060	43.1
	6.52	0.74	31	0.328	0.287	0.574	0.123	39.0
	6.59	0.73	21.5	0.277	0.328	0.565	0.124	41.0
	6.8	0.7	31.1	0.258	0.260	0.737	0.131	39.6
	6.66	0.72	21.9	0.244	0.244	0.750	0.132	42.2
Average values	6.7	0.73						
	6.60	0.076	21.5	0.095	0.163	0.775	0.027	34.2
	6.65	0.072	22.5	0.162		0.630	0.070	33.8
Average values	6.6	0.074						

It should be emphasized that the I_A values are initial absorbed intensities averaged from the readings taken at the beginning of the run and after sublimation of the calomel at the half-time point. The average intensity of radiation absorbed during the run would be about three-fourths of the reported I_A values.

The variation-in-intensity technique, described above, was used to study the effect of varying I_A on the Hg^{202} abundance, for several substrate pressures, at a constant flow rate of 2.7 ± 0.7 liter $minute^{-1}$. The data for substrate pressures of 0.27, 136, and 314 mm are shown in Table III. From Table II, data are available for the same flow rate at a substrate pressure of 7.2 mm. At the lowest pressures of 0.27 and 7.2 mm, the I_A values had to be corrected for incomplete quenching. Since the absorption path was only 0.1 cm, and the pressure of Hg^{202} was small, imprisonment of the hyperfine component was assumed to be negligible. The Stern–Volmer relation (7) should therefore be valid under these conditions. To make the correction the values of I_A, derived from the absorption data, were multiplied by $Z\tau/(1+Z\tau)$, where Z is the number of collisions per second of one Hg^{202} atom with the methyl chloride, and τ is the lifetime in seconds of the $Hg^{202}6(^3P_1)$ state. The Z values were calculated from Maxwell's collision frequency equation, with the collision cross section taken as the quenching cross section of methyl chloride for $Hg^N6(^3P_1)$ atoms. This value has been found by Darwent and Phibbs (8) to be 24×10^{-16} cm^2. The question of the magnitude of the lifetime, τ, of the $Hg^{202}6(^3P_1)$

TABLE III

The effect of pressure and absorbed intensity, at constant flow rate, on the Hg^{202} content of the solid product of the reaction of $Hg^{202}6(^3P_1)$ atoms, photoexcited in Hg^N, with methyl chloride

	Pressure, mm	Flow rate, liter min^{-1}	Saturation tempera-ture, ° C	Absorption		I_0	I_A	Hg^{202} abundance, atom %
				Initial	Half-time			
	0.27	1.99	19.5	0.436	0.526	0.072	0.012	37.4
	0.27	2.05	20.6	0.496	0.398	0.170	0.024	38.6
	0.27	2.15	20.0	0.375	0.412	0.545	0.038	41.1
	0.27	2.27	21.2	0.395	0.482	0.520	0.040	40.4
Average values	0.27	2.1						
	132	3.20	20.5	0.308	0.322	0.144	0.036	41.8
	135	3.18	20.0	0.328	0.311	0.194	0.049	42.8
	134	3.39	20.2	0.344	0.354	0.316	0.088	42.8
	142	3.29	20.2	0.350	0.338	0.555	0.148	45.4
Average values	136	3.3						
	312	1.60	21.3	0.252	0.320	0.070	0.032	37.9
	316	1.59	21.2	0.252	0.315	0.138	0.062	39.5
	313	1.53	20.0	0.256	0.292	0.545	0.117	40.7
Average values	314	1.6						

state has been discussed in an earlier paper in this series (1). For the lifetime of the $6(^3P_1)$ state of the even-mass mercury isotopes, Lennuier and Cojan (9) obtained 1.12×10^{-7} seconds. This value was used in the present calculations. The correction factors for incomplete quenching applied at the pressures of 0.27 and 7.2 mm were 0.19 and 0.88 respectively. It should be noted that the I_A values given in Table II are uncorrected for incomplete quenching.

The Hg^{202} abundance vs. I_A curves, corrected for incomplete quenching, are shown for the four pressures, 0.27, 7.2, 136, and 314 mm in Fig. 3. The enrichment-depressing effect of high substrate pressure is clearly shown at 314 mm. The values obtained in the 0.27–136 mm range all appear to fall on the same curve within the experimental error.

At low methyl chloride pressures, collisional transfer of energy between $Hg^{202}6(^3P_1)$ and Hg^N atoms could conceivably become important. From resonance radiation imprisonment measurements, Holstein, Alpert, and McCoubrey (10) have estimated that the mean quenching cross section of Hg^N is 10^{-13} cm^2. Knowing the quenching cross sections

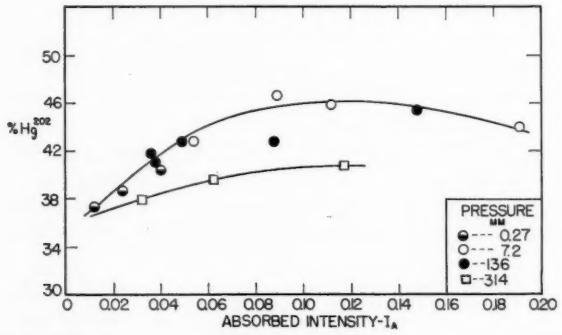

FIG. 3. The effect of I_A at constant flow rate on the abundance of Hg^{202} in the calomel product of the methyl chloride reaction at four substrate pressures.

of Hg^N and methyl chloride, it is possible to obtain the relative quenching of $Hg^{202}6(^3P_1)$ by Hg^N and methyl chloride from the collision frequency equation. At the lowest substrate pressure used, i.e. 0.27 mm, and with a mercury vapor pressure corresponding to equilibrium at 21° C, it was calculated that 99% of the $Hg^{202}6(^3P_1)$ atoms were quenched by methyl chloride. Quenching by Hg^N atoms was therefore considered negligible in the present investigation.

In all of the experiments reported in this paper on the effect of various reaction parameters on the Hg^{202} abundance, a consistent procedure was used in treating the reaction cell between experiments. Following the removal of the calomel product by solution in boiling concentrated hydrochloric acid, the cell was cleaned in aqua regia, to remove any traces of calomel or mercury, rinsed in distilled water, dried at 120° C, and heated to a dull red with a gas–oxygen flame. The flaming served to burn off any polymeric material formed on the cell during reaction. With repeated use it was observed that the transmission of the cleaned, Hg^N-free, cell slowly decreased. To improve the transmission, the cell was immersed in concentrated hydrofluoric acid for 30 minutes, rinsed, dried, and flamed. The transmission, following this treatment, was considerably higher. However, the Hg^{202} content of the calomels formed in succeeding experiments was found to be lower than before the treatment.

In order to determine whether surface factors influenced the Hg^{202} abundance, a series of 10 consecutive runs were performed, on the same cell, and under essentially the same reaction conditions. The runs differed only in the method of cell treatment between successive experiments. The data are summarized in Table IV.

It is apparent from the data that the aqua regia treatment, followed by flaming, is necessary to obtain maximum enrichments reproducibly. Furthermore, it appears that

TABLE IV

The effect of cell-cleaning methods in consecutive runs under constant reaction conditions on the Hg^{202} content of the solid product of the reaction of $Hg^{202}6(^3P_1)$ atoms, photoexcited in Hg^N, with methyl chloride

Cell treatment	Pressure, mm	Flow rate, liter min^{-1}	Saturation temperature, ° C	Absorption		I_0.	I_A	Hg^{202} abundance, atom %
				Initial	Half-time			
30 minutes in conc. HF, rinsed, dried, flamed	6.77	25.4	20.5	0.316	0.380	0.580	0.163	46.6
Cell flamed only	6.87	26.5	20.5	0.315	0.340	0.290	0.076	40.8
Cell flamed only	6.45	25.8	20.1	0.408	0.418	0.617	0.203	46.6
Cell cleaned in aqua regia, rinsed, dried, flamed	6.80	23.5	21.2	0.402	0.394	0.630	0.200	48.9
No treatment	6.42	24.9	21.0	0.414	0.428	0.650	0.213	40.5
No treatment	7.20	19.8	20.7	0.377	0.418	0.604	0.190	43.4
Cell cleaned in aqua regia, rinsed, dried, flamed	6.74	20.6	20.5	0.363	0.370	0.618	0.181	43.6
Cell cleaned in aqua regia, rinsed, dried, flamed	6.45	25.2	19.5	0.338	0.408	0.582	0.171	49.1
Cell cleaned in aqua regia, rinsed, dried, flamed	6.32	21.8	20.7	0.285	0.305	0.291	0.068	47.3
Cell cleaned in aqua regia, rinsed, dried, flamed	6.58	21.2	30.6	0.428	0.444	0.590	0.206	49.8

the "recovery" of the cell surface from other treatments is not immediate. In the last five runs in Table IV it can be seen that the untreated cell does not yield high values for the enrichment until two runs have been performed using the aqua regia method.

The possibility of isotopic degradation in the calomel product by gas-phase exchange reactions between $Hg^{202}Cl$ and Hg^{N} has been considered in an earlier study in this series (2) on the reaction of $Hg^{202}6(^3P_1)$ atoms with hydrogen chloride – butadiene mixtures. It was found that repeated sublimation of the calomel product did not alter the Hg^{202} abundance, compared to that for unsublimed calomel.

In this investigation, exchange between Hg^{N} vapor and isotopically enriched solid calomel was examined. A deposit of enriched calomel was first laid down in the cell under the following reaction conditions: 6.87 mm pressure of methyl chloride, at a flow rate of 0.7 liter minute^{-1}, a saturation temperature of 20° C, and an absorbed intensity of 0.159. The lamp was then turned off, and the Hg^{N}-saturated methyl chloride was allowed to flow through the cell for an additional 30 minutes. The Hg^{202} abundance was found to be 40.8%, the value to be expected under the conditions of the experiment. This experiment would suggest that exchange between gaseous Hg^{N} and isotopically enriched solid calomel is not significant under the conditions of this investigation.

The reaction between photoexcited Hg^{202} atoms and solid calomel is another exchange reaction which could be influential in determining the Hg^{202} abundance. This possibility was investigated by depositing a layer of $Hg^{N}{}_2Cl_2$ by irradiating the Hg^{N}-saturated stream of methyl chloride with an electrodeless discharge source containing Hg^{N}. The deposit was sublimed from the cell face and the system was evacuated. A stream of nitrogen, presaturated with Hg^{N}, was then allowed to flow through the system, under irradiation with the Hg^{202} source. After 30 minutes the run was stopped and the mercury from the calomel was analyzed. An Hg^{202} content of 29.7% was found, corresponding to the natural abundance. This experiment would suggest that neither $Hg^{202}6(^3P_1)$ atoms nor $Hg^{202}6(^3P_0)$ atoms can displace the mercury atoms in solid calomel.

The effect on the Hg^{202} enrichment of adding unsaturated hydrocarbons to the methyl chloride stream was studied using propylene and butene-1 as addends. The data are summarized in Table V. In this table the I_A values given were determined as described above. The numbers are proportional to the absorbed intensity for the Hg^{N}-saturated gas mixture. The fraction of I_A partitioned in competitive quenching to methyl chloride is designated in Table V as $I_A(CH_3Cl)$. To obtain $I_A(CH_3Cl)$, the I_A values were multiplied by the relative quenching factor $[Z(CH_3Cl)/Z(G)]/[1+Z(CH_3Cl)/Z(G)]$: where $Z(CH_3Cl)$ and $Z(G)$ represent respectively the number of collisions between Hg^{202} and methyl chloride and between Hg^{202} and the added gas. For calculating the collision frequency ratio, quenching cross sections of 31 and 33.5×10^{-16} cm^2 were used respectively for propylene and butene-1 (11). In addition to the correction of I_A for competitive quenching, the fraction of light escaping by resonance fluorescence was also considered.

From Table V, it can be seen that the addition of propylene and butene-1 has a slightly depressing effect on the Hg^{202} content in comparison with the value for the pure substrate, under comparable conditions. From the four runs with varying concentrations of butene-1, it would appear that the enrichment-depressing effect of this addend decreases with increasing concentration.

As a preliminary study on the effect of the alkyl side chain on the isotopically specific reaction, a series of 19 runs was done with isopropyl chloride as substrate. Reaction pressure was varied from 0.16 to 308 mm, and the flow rate from 0.0007 to 11.20 liter minute^{-1}.

TABLE V

The effect of added gases on the Hg^{202} content of the solid product of the reaction of $Hg^{202}6(^3P_1)$ atoms, photoexcited in Hg^N, with methyl chloride at a flow rate of 20.5 ± 1.5 liter $minute^{-1}$

Added gas	P (Total), mm	P (CH_3Cl), mm	P, mm	% added gas	I_A	I_A (CH_3Cl)	Hg^{202} abundance, atom %
Propylene	4.89	3.46	1.43	28.3	0.175	0.093	42.2
Propylene	4.90	3.53	1.37	28.0	0.175	0.095	44.2
Butene-1	5.51	3.47	2.04	37.0	0.202	0.110	42.0
Butene-1	4.63	3.06	1.57	33.8	0.233	0.113	41.4
Butene-1	4.69	4.28	0.41	8.7	0.222	0.149	40.4
Butene-1	4.76	4.35	0.41	8.6	0.133	0.099	38.5
None	4.63	4.63	0	0	0.130	0.130	44.0

As with methyl chloride, maximum enrichments were obtained at low pressures and high flow rates. The highest Hg^{202} abundance was 44.1%, for a pressure of 6.42 mm and a flow rate of 8.0 liter $minute^{-1}$. This point fits on the curve for methyl chloride, shown in Fig. 1, for the same saturation temperature of 20° C.

DISCUSSION

In a previous paper (2) in this series, on the reaction of $Hg^{202}6(^3P_1)$ atoms, in Hg^N, with hydrogen chloride, it was pointed out that there are two factors which must be considered before the significance of reaction parameters in the kinetics can be properly assessed. These factors are (*a*) the Lorentz-broadening effects of substrate pressure on the hyperfine absorption contours, and (*b*) the depletion in Hg^{202} of the Hg^N present in the reaction zone through isotopically specific processes. These factors will first be discussed.

By analogy with the hydrogen chloride reaction (2), the formation of a calomel product, enriched in Hg^{202}, in the reaction of methyl chloride with $Hg6(^3P_1)$ atoms, in Hg^N, could be ascribed to the sequence:

$$CH_3Cl + Hg^{202}6(^3P_1) \rightarrow CH_3 + Hg^{202}Cl \quad [1]$$

$$CH_3Cl + Hg^{202}6(^3P_1) \rightarrow CH_3 + Cl + Hg^{202}6(^1S_0) \quad [2]$$

$$Hg^N + Cl + M \rightarrow Hg^NCl + M \quad [3]$$

where M represents a third body in the gas phase, or the wall.

The Lorentz-broadening effects of methyl chloride on the five absorption contours of the 2537 Å line of Hg^N have been discussed in some detail in a previous paper (1). Quantitative estimates were there made of the fraction of Hg^{202} resonance radiation absorbed by Hg^N with increasing methyl chloride pressure. From these data, and the Hg^{202} abundances in the present investigation, an approximate calculation can be made of the magnitude of the Lorentz effect in the methyl chloride reaction. On the basis of the three-step mechanism above, the ratio, R, of the rates of $Hg^{202}Cl$ to Hg^NCl formation is related to the fractional Hg^{202} abundance, α, in the calomel product by the equation:

$$R = (\alpha - 0.298)/(1-\alpha),$$

where 0.298 is the α value for natural mercury. The calculation can only be made for low I_A values, under which conditions Hg^{202} depletion of the Hg^N in the irradiated zone should be negligible, as required by reaction [3]. From Fig. 3 it can be seen that at substrate pressures less than 136 mm, there is no appreciable pressure effect on the Hg^{202} enrichments, since the abundance values all lie on the same curve within the

experimental error. From this curve the value of $\alpha = 0.44$, for $I_A = 0.06$; whence, from the above equation, $R = 0.25_4$. From reference 1 the fraction of incident Hg^{202} radiation absorbed by Hg^{202} atoms, at a methyl chloride pressure of 314 mm, is 0.70. The apparent R value at this substrate pressure will therefore be $(0.70)(0.25_4) = 0.17_8$. Substituting this value in the above equation an α value of 0.40 is obtained. From Fig. 3, the experimental value is 0.395, for $I_A = 0.06$ and $P = 314$ mm.

From the above calculation, the Lorentz effect would appear sufficient to account for the decrease in Hg^{202} abundance at high substrate pressures. This subject will be dealt with in greater detail in forthcoming papers from this program.

From Fig. 2, it would appear that the Hg^{202} abundances, at a fixed flow rate, increase with increasing I_A to a maximum value and then fall off. The maximum value becomes progressively greater with increasing flow rate. This behavior can be adequately explained in terms of a localized depletion of the Hg^{202} content of the Hg^N in the reaction zone through reaction [1]. Under such conditions reaction [3] takes place with mercury containing less than the normal abundance (29.8%) of Hg^{202}. The net Hg^{202} enrichment found in the recovered calomel will thereby be reduced. This depletion effect would be minimized at high flow rates and low I_A values. The extreme case of Hg^{202} depletion would of course occur under static conditions. Here a calomel containing the normal Hg^{202} abundance was recovered. The static behavior points up the fact that the photochemical reaction is very much faster than the rate of evaporation of the liquid Hg^N present in the reaction cell. All of the Hg^N present must be consumed in primary and secondary calomel-forming reactions in order for Hg^NCl to be recovered.

Since the relative mean absorbed intensities (I_A) were determined under reaction conditions, the net decrease in the Hg^{202} content of the Hg^N with decreasing flow rate can be calculated. In Table II, the three sets of runs at flow rates of 23.8, 0.73, and 0.074 liter minute^{-1} were performed consecutively with the same reaction cell. For each set the A values were averaged and the corresponding mean concentrations of Hg^{202} were obtained from the calibration curve of the absorbiometric analysis unit (6). The results of the calculations are shown in Table VI, with the mean Hg^{202} concentrations

TABLE VI

The effect of flow rate on the concentration of Hg^{202} atoms in the reaction zone, in the reaction of $Hg^{202}6(^3P_1)$ atoms in Hg^N with methyl chloride

Flow rate, liter minute^{-1}	Average absorption	N^{202}, atoms cm$^{-3}\times10^{-13}$	Equilibrium temp., ° C
23.8	0.335	1.45	21.2
0.73	0.231	0.93	16.1
0.074	0.128	0.52	9.8

(N^{202}) given as the number of Hg^{202} atoms per cc. The progressive decline in the N^{202} values with decreasing flow rate is clearly evident. In the last column of Table VI the equilibrium temperatures of liquid Hg^N are given corresponding to the vapor concentrations of Hg^N indicated by the N^{202} values. At the highest flow rate (23.8 liter minute^{-1}), the equilibrium temperature corresponds, within the experimental error, to the temperature of the exit condenser of the mercury saturator. However, at the lowest flow rate (0.074 liter minute^{-1}) the equilibrium temperature is 11.4° C below the saturator temperature. These calculations show up clearly the Hg^{202}-depleting effect of reaction [1] on the Hg^N in the light zone. It should further be noted that these results prove the efficiency

of the method used for saturating the gas stream with Hg^N. This is evident from the fact that the equilibrium temperature is the same as the saturation temperature at the highest flow rate employed.

From the preceding considerations, it seems reasonable to conclude that the Hg^{202} abundances in the methyl chloride reaction are invariant in both substrate pressure and volume flow rate when the actual data are corrected for Lorentz-broadening of the hyperfine absorption contours and depletion of Hg^{202} in the Hg^N present during reaction.

The specific nature of the primary processes occurring in the reaction of methyl chloride with $Hg^{202}6(^3P_1)$ atoms was the focus of interest in this study. Pertinent to this, the quenching cross section of methane for $Hg^N6(^3P_1)$ atoms is only 0.08×10^{-16} cm^2 (7), whereas that of methyl chloride is 24×10^{-16} cm^2 (8). The substitution of chlorine in the methane molecule results therefore in well over a 300-fold increase in quenching cross section. From these data alone one would expect that chemical quenching would occur almost exclusively at the C—Cl bond in methyl chloride. In their study of the methyl chloride reaction with $Hg^N6(^3P_1)$ atoms, at elevated temperatures, Masson and Steacie (3) came to this conclusion on the basis of the nature and quantum yields of the products formed. The results of the present work substantiate this conclusion and show further that at least part of the calomel product recovered originates in the primary quenching reaction. It should be emphasized that this study indicates primary calomel formation in the room temperature reaction. It would be expected that increasing reaction temperature would favor reaction [2] over reaction [1]. Hence our results are not necessarily in disagreement with the conclusions of Masson and Steacie (3) that the primary process is exclusively reaction [2] at elevated temperatures.

From the fact that the calomel recovered is not pure $Hg^{202}Cl$, it would appear necessary to postulate the two primary processes, [1] and [2], to allow for secondary Hg^NCl as well as primary $Hg^{202}Cl$ formation. That calomel is forming by secondary reactions is clearly indicated by the effect of flow rate and intensity, discussed above, on the Hg^{202} abundance. Further evidence for reaction [2] has recently been obtained in further studies on the methyl chloride reaction (12). It has been found that hydrogen chloride is an important product of the reaction at room temperature. The presence of this product can be most readily explained by the reaction:

$$Cl + CH_3Cl \rightarrow HCl + CH_2Cl. \qquad [4]$$

This step has been previously postulated by Masson and Steacie (3) to explain HCl formation in the reaction at higher temperatures. It is likely that the two primary processes involve a common intermediate, since reaction parameters do not appear to influence the ratio of the rates of the two processes.

To this point it has been implied that secondary Hg^NCl formation arises by direct reaction of Cl atoms with Hg^N in the presence of a third body, as shown in reaction [3]. For their higher temperature conditions, Masson and Steacie (3) concluded that calomel formed by the reaction:

$$CH_2Cl + Hg^N \rightarrow Hg^NCl + CH_2. \qquad [5]$$

In the present investigation, CH_2Cl radicals will be available not only through reaction [4] but also from abstraction reactions of methyl radicals, formed in [1] and [2], with the substrate (13):

$$CH_3 + CH_3Cl \rightarrow CH_4 + CH_2Cl. \qquad [6]$$

It would be expected that these radicals would be consumed mainly through recombination (3):

$$2CH_2Cl \rightarrow C_2H_4Cl_2. \qquad [7]$$

With increasing I_A, there would be a localized build-up in Cl atom concentration, favoring reactions [3] and [4]. This should result in no net change in the Hg^{202} abundances, since $Hg^{202}Cl$ is simultaneously being formed in reaction [1]. However, if $Hg^{N}Cl$ is also being formed by [5], and since any increase in I_A will enhance the steady-state concentration of CH_2Cl radicals, the rate of $Hg^{N}Cl$ formation will increase more rapidly than that for $Hg^{202}Cl$ formation, with a resulting decrease in the Hg^{202} content of the recovered calomel. This is contrary to our findings, since actually an increase in Hg^{202} content was observed with increasing I_A. It appears therefore unlikely that reaction [5] is significant under our reaction conditions. It should further be noted that a similar intensity effect was found in the reaction of $Hg^{202}6(^3P_1)$ atoms in Hg^{N} with hydrogen chloride – butadiene mixtures (2).

It is possible that the reason for the positive intensity effect should be sought in the nature of reaction [3]. With increasing I_A, the localized enhancement of Cl atom concentration may result in a decreased efficiency in reaction [3] through its third-body restriction. Any reduction in the efficiency of [3] would result in a net increase in the Hg^{202} content of the recovered calomel.

From Table V it can be seen that the addition of propylene or butene-1 to the methyl chloride stream results either in no change or a slight decrease in the Hg^{202} content of the recovered calomel. While it is likely that these addends are slightly more efficient than methyl chloride in removing Cl atoms, any beneficial effect of this type in suppressing $Hg^{N}Cl$ formation will be compensated by a decreased I_A partitioned to the methyl chloride through competitive quenching effects from the added olefins.

The influence of cell-cleaning techniques on the Hg^{202} abundance is summarized in Table IV. The behavior suggests that isotope exchange reactions in product recovery may be playing a role in determining the Hg^{202} abundance found in the mercury recovered from the calomel product. Thus the physical condition of the cell surface may determine the extent to which Hg^{N} adsorbs upon it. In the recovery of Hg^{202}-enriched mercury from the calomel the importance of isotopic degradation through exchange reactions between Hg^{202} ions and Hg^{N} will be determined by the quantity of Hg^{N} adsorbed on the calomel product. This problem has been discussed in an earlier publication (14). The importance of exchange reactions in investigations of this type is currently being studied in the laboratories of one of us (HEG).

From the preliminary study of the isopropyl chloride reaction there is no evidence that an increase in the carbon chain length has any influence on the enrichment process.

CONCLUSIONS

As a result of this investigation it can be concluded that $Hg6(^3P_1)$ atoms react with alkyl chlorides through two primary modes:

$$RCl + Hg6(^3P_1) \rightarrow HgCl + R$$

$$RCl + Hg6(^3P_1) \rightarrow R + Cl + Hg6(^1S_0).$$

Through the technique of initiating the photosensitized decomposition with $Hg^{202}6(^3P_1)$ atoms in Hg^{N}, it has been possible to show that the calomel product is formed partially in the primary quenching reaction, and partially by secondary reactions of the type:

$$Cl + Hg + M \rightarrow HgCl + M.$$

The two primary modes of decomposition presumably involve the same short-lived intermediate in which the mercury atom is associated with the chlorine of the alkyl chloride. For alkyl halides in general the scission of the intermediate R—X—Hg into HgX and R would presumably be favored with increasing bond strength of the HgX. For this reason studies are now in progress in the laboratories of one of us (HEG) on the reaction of $Hg^{202}6(^3P_1)$ atoms in Hg^N with alkyl fluorides. Here it is conceivable that higher Hg^{202} enrichments would be obtained because of the greater stability of HgF compared to HgCl.

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THE MECHANISMS OF OXYMERCURATION[1]

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ABSTRACT

The oxymercuration of norbornenes has been found to be acid-catalyzed, and to give oxymercurials which have a higher dipole moment and greater stability toward deoxymercuration than do their diastereomers in which the configuration of the mercuri linkage has been inverted. Since these properties can be correlated with those of the oxymercurials from norbornenedicarboxylic acids (partly published heretofore and elaborated in the present report) the configurations of which are known, it follows that the configurations of the oxymercurials from norbornene are ↑↓ (*trans*). But these configurations must be opposite to those of the oxymercurials from cyclohexene, cyclopentene, α-terpineol, and the geoisomeric stilbenes, the formations of which are not acid-catalyzed and the dipole moments of which are lower than those of the diastereomers inverted with respect to the mercuri linkage. The configuration of these oxymercurials must be ↓↓ (*cis*) and the mechanism of their formation must be different from the acid-catalyzed oxymercuration of norbornene. The mechanism for *cis* (↓↓) addition has previously been suggested as non-ionic. Calculation of the electric moments of these ↓↓ diastereomers shows that hindrance to group rotation must prevail. It is reasonable to attribute the relative ease with which they may be deoxymercurated to this hindrance.

For some years there has been a difference of opinion in respect of the mechanism whereby the elements of hydroxy- or alkoxy-mercuric salts add to alkenes. This controversy is of interest beyond that of the oxymercurials because oxymercuration may provide an insight of alkene reactions not provided by less definitive reactions of these hydrocarbons. Thus it has been observed that oxymercuration is generally entirely stereospecific, with simple second-order kinetics in which a *cis*-geometric isomer is oxymercurated at a faster rate than is its *trans*-modification. However, none of these characteristics define the mechanism of reaction.

In 1935 the reaction was specified as an addition of molecular hydroxy- or alkoxymercuric acetate to the carbon–carbon double bond (1), and this belief that the added groups were in contiguous (so-called *cis*) configuration was reiterated in 1947 (2). Meanwhile, the alternative postulation has been made (3) that an ionized alkane–mercurinium salt is first formed from an ionizable mercuric salt and an alkene. The cation of this salt is subsequently attacked by a nucleophilic hydroxide or alkoxide ion, with inversion, to produce the oxymercurial in which the added groups are in the non-contiguous (so-called *trans*) relationship to one another. This mechanism is portrayed here for the oxymercuration of 1,4-methylene-Δ^2-cyclohexene (norbornene, I).

It might be predicted from this mechanism that the reaction would be favored by a system in which the ionization of mercuric salts would be enhanced. Moreover, the prevalence of the two possible products, 3-↓-methoxy-1,4-↑↑-methylenecyclohexyl-2-↑-mercuric salt (IV) versus 3-↓-acetoxy-1,4-↑↑-methylenecyclohexyl-2-↑-mercuric salt (III), ought to depend upon the relative activities of the anions $X^{\ominus}$ (usually acetate) and $OCH_3^{\ominus}$ in the system.

The oxymercuration of norbornene, I, has been found to conform with these predictions. A quantitative yield of III is formed rapidly when I is treated with mercuric acetate (X = OAc) in acetic acid. More specifically, a 0.34 molar solution of mercuric acetate in 2,5-dioxahexane converts 1 equivalent of norbornene into nearly pure 3-↓-acetoxy-1,4-↑↑-methylenecyclohexyl-2-↑-mercuric salt (III, X = Cl after treatment with aqueous sodium chloride, m.p. 126–128°) in 98% yield during 30 minutes. Neither rate

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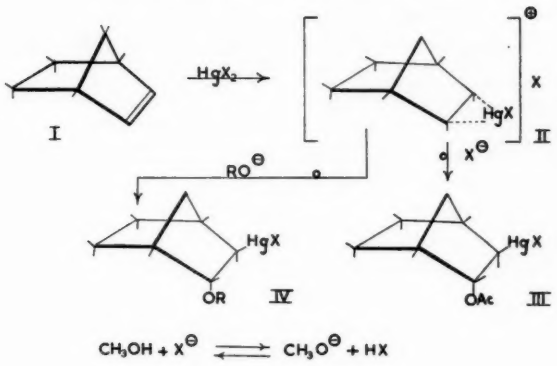


nor yield is diminished by inclusion of either 1 or 0.1 equivalent of boron fluoride etherate, although 0.1 equivalent of pyridine decreases the yield to 62% and 1 equivalent to 24% during 30 minutes. The effect of pyridine may be expected because of its tendency to coordinate with mercuric salts.

The configuration of this oxymercurial has been studied. The position of the acetoxy group in III (X = Cl) has been proved by saponification to be 3-↓-hydroxy-1,4-↑↑-methylene-2-↑-cyclohexylmercuric chloride (IV, R = H). This substance may be reduced by use of hydrazine hydrate in large excess to 3-↓-hydroxy-1,4-↑↑-methylenecyclohexane, identical with that obtained by Alder, Stein, and Rickert (4, 5) and configurationally established by Alder and Windemuth (6). The position of the chloromercuri group seems to be *trans* (↑) with respect to the acetoxy substituent according to the comparatively high dipole moment (3.6 Debye) which III (X = Cl) displays in dioxane. Therefore, the oxymercuration seems to have occurred via the alkane–mercurinium salt, II.

The same mode of reaction seems to occur when an equivalent of methanol is included with the mercuric acetate and norbornene in 2,5-dioxahexane but the product is IV (R = CH_3), as might be expected if methoxide ion were strongly nucleophilic in this medium. The configuration of 3-↓-methoxy-1,4-↑↑-methylene-2-↑-cyclohexylmercuric chloride (IV) corresponds with that of III because the 3-↓-hydroxy analogue to which III has been converted may be methylated in good yield (7) to the methoxy analogue, IV.

In protonic media the oxymercuration of norbornene is less simple. In water a mixture of III and IV (R = H, X = Cl after sodium chloride treatment) is obtained from which pure IV may be obtained by saponification. In methanolic solution, 0.00025 molar in I, and mercuric acetate a 97% yield of a mixture comprising 65% of IV (R = CH_3) and 35% of III is obtained. This behavior, not usual in the preparation of oxymercurials, would seem to be due to competition in nucleophilic attack of an intermediate like II by alkoxide and acetate ions. The following experiments substantiate this belief.

In Table I, items 1 to 4, is shown a series of experiments in which the molarity of norbornene and mercuric acetate in methanol has been lowered by dilution with this solvent. The products from these 90-minute experiments have been analyzed by melting point – composition diagram and by acetyl determinations.

It may be seen that upon increased dilution the yield is first increased and then essentially is constant. Of greater significance is the increasing amount of methoxymercurial (IV) instead of acetate (III) in the product. Item 11 shows that this tendency is independent of the absolute quantity of mercuric acetate in the system, although item 12, like

TABLE I

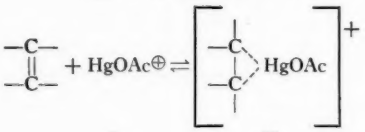
Oxymercuration of norbornene by mercuric acetate in methanol during 90 minutes followed by dilution into aqueous sodium chloride (X = Cl)

Item	Molarity of I and $Hg(OAc)_2$ in MeOH $\times 10^3$	Excess equiv. $Hg(OAc)_2$	Equiv. NaOAc	Equiv. HOAc	Total yield, %	% IV in total
1	0.5				86	61
2	0.25				97	66
3	0.1				93	73
4	0.07				95	86
5	0.25			1	85	80
6	0.25			5	69	73
7	0.25			20	69	67
8	0.25		1		73	21
9	0.25		2		60	15
10	0.25		10		81	10
11	0.04	9			99	90
12	0.12	3			90	60

item 1, shows that a high ratio of mercuric acetate to norbornene tends to decrease the formation of IV in favor of III. These behaviors might be expected if formation of methoxide ion were a consequence of equation [i] to which the reaction of equation [i] furnished little acetate because of limited dissociation.

Consideration of equations [i]–[vii] permits explanation of the results shown in Table I.

$$Hg(OAc)_2 \rightleftharpoons HgOAc^{\oplus} + OAc^{\ominus} \qquad [i]$$

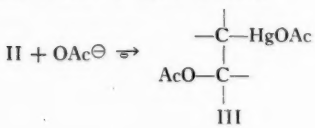


[ii]

I II

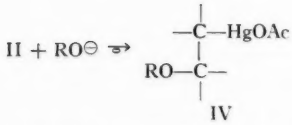
$$HOAc \rightleftharpoons H^{\oplus} + OAc^{\ominus} \qquad [iii]$$

$$ROH + OAc^{\ominus} \rightleftharpoons RO^{\ominus} + HOAc \qquad [iv]$$



[v]

III



[vi]

IV

$$Hg(OAc)_2 + ROH \rightleftharpoons RO-HgOAc + HOAc \qquad [vii]$$

$$HgO + 2HOAc \rightarrow Hg(OAc)_2 + H_2O \qquad [viii]$$

The reaction involving norbornene (I), mercuric acetate, and methanol may be adequately described by these equations. Dilution of the solution of reactants with methanol as indicated in items 1–4, Table I, would result in increased formation of methoxide ion and reduction of acetate ion by equation [iv]; thus favoring the formation of IV as described by equation [vi] at the expense of formation of III by equation [v]. Reduction of acetate ion would result in increased formation of the acetoxymercurinium ion (equa-

tion [i]). Thus increased dilution of the reactants with methanol would favor increased ionization of the mercuric acetate and would result in an increased yield of III plus IV in 90 minutes.

An equilibrium shift of the reaction described by equation [i] ought to be enhanced more by the ionization of acetic acid than by mercuric acetate. This expectation is realized in item 5 and to a certain extent in item 6, by comparison with item 2, but item 7 shows when addition of acetic acid reaches the 20-equivalent level the presence of acetate ion starts to favor the formation of III to the detriment of IV.

Inclusion of varying amounts of acetic acid (items 5–7, Table I) should reduce the over-all per cent yield in 90 minutes. The reason for this reduction is readily found by interpretation of equations [i]–[vii]. The increase in the ratio of III:IV produced by addition of acetic acid (and thus increased acetate ion) is explicable by consideration of the ratio, acetate:methoxide ion.

Inclusion of sodium acetate, a salt highly ionized in methanol compared with acetic acid, should further enhance the effect observed with added acetic acid. Addition of 10 equivalents of sodium acetate (item 10) increases the amount of the acetoxymercurial III to 90% of the total product.

According to these evidences of ionic participation it would follow that conditions in which basic mercuric salts would be prevalent ought to decrease the rate of reaction. This condition has been devised by inclusion of mercuric oxide into the methanolic system 0.25 molar in norbornene and mercuric acetate. In this experiment, the reaction shown in equation [viii] would be operative together with the reactions described by equations [i]–[vii]. After 4 hours the total yield is only 70% but the acetic acid liberated from this amount of oxymercuration has by this time dissolved the suspended mercuric oxide. Subsequently the yield rises to 90%. Of interest is the observation that the 90% yield contains at least 10% more of the methoxymercurial than is obtained from the reaction system in which no mercuric oxide is present.

This evidence that methoxymercuration of norbornene is retarded in a basic or neutral environment would indicate that this reaction would be favored in acidic media. The data of Table II substantiate this prediction.

The addition of only 0.02 equivalent of sulphuric acid increases the amount of methoxymercurial, IV, relative to the acetate, III, from 67 to 85%. While the addition of larger amounts of sulphuric acid tends slightly to decrease the total yield (deoxymercuration), the percentage of IV in this total actually is increased. It would appear that the bisulphate ion, itself not sufficiently nucleophilic to undergo neutralizing addition to an alkane–mercurinium salt, removes acetate ion from the system according to equation [ix]. The behavior of methoxyfluoboric acid

$$Hg(OAc)_2 + H^{\oplus} + HSO_4^{\ominus} \leftrightarrows HgOAc^{\oplus} + HSO_4^{\ominus} + HOAc \qquad [ix]$$

and *p*-toluenesulphonic acid probably are similar. In this connection it may be observed that hydrochloric acid does not increase the yield of IV, undoubtedly because it is converted to mercuric chloride which is largely unionized.

It may be seen from the table that odd electron donors such as benzoquinone, hydroquinone, and *tert*-butylhydroperoxide are entirely ineffective. To be sure stannous chloride and ferrous sulphate are both effective for augmentation of IV over the acetate, III, but they may be functioning in formation of complex anions. The augmentation by the ferrous salt is of especial interest if the present findings are contrasted to an earlier report of the preparation of 3-methoxymethylenecyclohexylmercuric chloride (8) in which

TABLE II

The effect of catalysts on oxymercuration with norbornene and mercuric acetate 0.25 molar in methanol during 90 minutes

Catalyst	Equiv. of catalyst	Total yield, %	% of IV in product	
			From acetyl content	By thermal analysis
Sulphuric acid	0.02	92		85
	0.10	85	90	89
	0.50	85		93
	1.00	85		93
p-Toluenesulphonic acid hydrate	0.10	90	86	83
	2.5	95		95
Ferrous sulphate	0.05	75	80	79
Boron fluoride etherate	0.10	95	90	89
Stannous chloride	0.10	65	79	81
Hydroquinone	0.10	93		69
Benzoquinone	0.10	95		68
Hydrochloric acid	0.10	83		68
tert-Butylhydroperoxide	0.10	93		67
None		97		67
Pyridine	0.10	95	58	55
	1.00	89	37	30
Trimethylamine	0.10	90	24	21

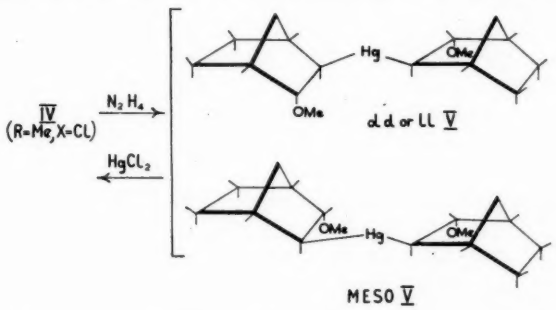
a good yield in high purity seemingly was obtained with a system comprised only of norbornene, mercuric acetate, and methanol. In view of our findings with this system, we presume that a contaminant such as ferrous salt must have been present in Rowland's system since otherwise he could not have obtained the high yield of methoxymercurial which he reported. Rather he should have obtained a mixture of III and IV.

In addition to the substances which accelerate the methoxymercuration over the formation of 3-↓-acetoxy-1,4-↑↑-methylenecyclohexyl-2-↑-mercuric salt (III), it may be seen from Table II that tertiary amines like pyridine and trimethylamine strongly retard methoxymercuration in favor of the formation of III. This must be due to the augmentation of acetate ion from the acetic acid formed in the system. Of course these nitrogen-containing electron-donors have been known previously to retard methoxymercuration, and earlier in this report it was shown that pyridine retarded the formation of III in 2,5-dioxahexane. Probably these latter effects are inconsequential to the argument of Table II. It may be seen that the presence of the amines did not appreciably diminish the total yield in methanol. Actually, the effect of either acids or bases on the rate of norbornene oxymercuration has not been evaluated in the present study because the reaction, even without addends, is very fast. Although 90 minutes has been allowed in these studies in order that all reactions would be standardized with respect to time, it is known that the 0.25 molar reaction in methanol at 20° C is complete within 45 seconds.

One may ask how this evidence for an ionic mechanism of oxymercuration may be correlated with previous experience of the general reaction. For example, it has been shown (9) that acetic acid retards one oxymercuration while the removal of acetic acid by evaporation from another, typical, reaction increases the rate (10). Moreover the evidence for ↑↑ (*cis*) addition is strong in respect of general oxymercuration (11), except for an X-ray diffraction study (12) which may be questioned in view of recent opinions about the flexibility of the cyclohexane ring. In view of these experiences the present results might seem to be anomalous.

An explanation has been sought, and found, in the chemical and physical properties of the norbornene methoxymercurials. First, the stability of the product designated as 3-↓-methoxy-1,4-↑↑-methylenecyclohexyl-2-↑-mercuric chloride (IV, R = Me, X = Cl) is unusually high. This stability is apparent also in the products obtained when IV is treated with excess hydrazine hydrate. For the first time this reaction has yielded methoxyalkyl bis-mercurials; both diastereomers have been obtained as solids which were separable by fractional crystallization. Either diastereomer can be reconverted to the original chloromercurial, IV, so that the reconversion of the bis-mercurial is stereospecific. We consider the higher melting (108°) bis-mercurial to be the meso isomer, V; also it has the higher dipole moment (2.17 D in benzene).

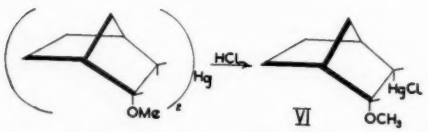
A second evidence of the stability of IV has been observed by the diastereomeric equilibration of IV (↓↑) with its isomer (↓↓, VI) with a small amount of hydrazine hydrate. This reaction has been shown (13) to give diastereomeric mixtures of 2-oxycyclohexyl and 2-oxycyclopentyl mercurials. The more stable diastereomer in the mixture may be isolated by treatment with methanolic hydrogen chloride which deoxymercurates the other diastereomer. The recovered diastereomer, which has been designated as β, has always heretofore been that one *not* obtained by oxymercuration of the alkene.



In contrast, the diastereomer recovered by partial deoxymercuration of the mixture of IV and VI is IV, the product of oxymercuration, in good yield. In order to isolate VI (at best, in small amount) an arduous fractional crystallization of the IV–VI mixture is required. This separation may be facilitated slightly by first converting the IV–VI mixture into a bis-mercurial mixture containing all four diastereomers, of which V represents a pair. This is accomplished by treatment of the IV–VI mixture with excess of hydrazine hydrate. When the four-diastereomer mixture is treated cautiously with less than the stoichiometric amount of methanolic hydrogen chloride for the reaction, the amount of VI in the mixture of IV and VI has been enhanced. Probably steric effects have altered the relative rates of diastereomeric scission.

The properties of VI do not resemble those of the previously known cyclic β-chloromercurials. It has been pointed out above that VI is more easily deoxymercurated than is IV, and this contrast to other cyclic α=β pairs is confirmed by the observation that the dipole moment of VI is found to be lower than that of IV. It would seem from these properties that the configurations of the norbornene oxymercurials are opposite to those of other oxymercurials such as are prepared from terpineol (14), cyclopentene (13), and cyclohexene (13, 15).

According to this definition of the configurations those assigned by Winstein, Traylor, and Garner (15) must be incorrect.



4 DIAST. MIXTURE plus IV (VI)

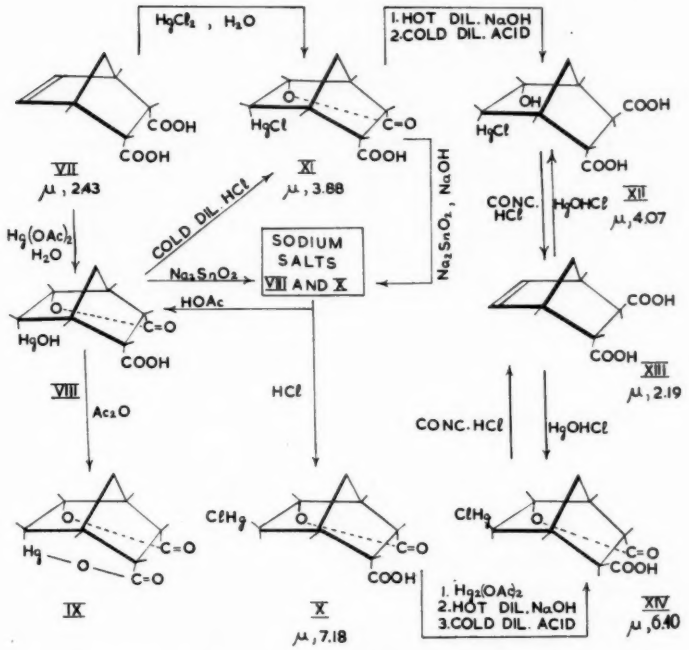
plus NORBORNANE

In contrast to the oxymercurations of cyclopentene and cyclohexene it may be said that the oxymercuration of norbornene is abnormal. This unusual behavior may not be unexpected in view of the dipole moments observed (Table III) for norbornane and norbornene, which would indicate a displacement of the electronic fields in these substances. Moreover, it has been shown previously (16, 17) that bromination of the norbornene-2,3-dicarboxylic acids does not follow the common ↑↓ addition of bromine to the double bond. During the remainder of this report it will be shown that some of these dicarboxylic acids also are abnormal in respect of oxymercuration.

During our previous work (11) with 1,4-↑↑-methylene-Δ^5-cyclohexene-2,3-↓↓-dicarboxylic acid (endo-norbornene-2,3-dicarboxylic acid, VII) we did not discern any abnormality when we established the *cis* (↓↓) configuration for the product (VIII) obtained by treatment of VII with aqueous mercuric acetate. Although the compound shown graphically as VIII could, alternatively, be 5-↓-hydroxy-anhydro-[6-↓-hydroxymercuri-2-↓-carboxy]-1,4-↑↑-methylenecyclohexane-3-↓-carboxylic acid, the choice of which transannular bridge is open is configurationally unimportant. Either form would be expected to undergo dehydration upon treatment with acetic anhydride to give 5-↓-hydroxy-anhydro-[6-hydroxymercuri-2-↓-carboxy]-1,4-↑↑-methylenecyclohexane-3-↓-carboxylic acid, γ-lactone (IX). The configuration of IX (and therefore of VIII) must be ↓↓ in respect of the oxy- and mercuri-linkages because its molecular weight has been determined cryoscopically as 381. The calculated molecular weight of IX is 382, so a polyester structure is not involved. The configuration of VIII and IX must therefore be ↓↓ as well.

It may be expected that the chloromercurial XI derived from VIII by acidification with hydrochloric acid also will have the ↓↓ configuration. But XI may be obtained directly by treatment of the unsaturated acid, VII, with mercuric chloride in water. This observation by Mr. J. H. Robson marks the first instance of oxymercuration in which participation of a basic mercuric salt cannot be postulated. Indeed, the near-quantitative yield is only lowered by 15% when 2 equivalents of hydrogen chloride are included with the mercuric chloride, although the otherwise very rapid reaction is retarded by this extra acid. The behavior is strongly suggestive of an ionic reaction which will be discussed later in this report.

When either VIII or IX is treated with aqueous sodium stannite the expected precipitation of metallic mercury occurs, and this presumably homopolar reaction (18) yields a diastereomeric mixture. Careful acidification with acetic acid precipitates VIII, perhaps in the anhydromercurial form mentioned above. After removal of VIII the filtrate may be acidified further by use of hydrochloric acid to yield the diastereomeric 5-↓-hydroxy-6-↑-chloromercuri-1,4-↑↑-methylenecyclohexane-2,3-↓↓-dicarboxylic acid, γ-lactone (X). This compound may be deoxymercurated (by treatment with concentrated hydrochloric acid) to the same 5-↓-hydroxy-1,4-↑↑-methylenecyclohexane-2,3-↓↓-di-



carboxylic acid, γ-lactone, obtained (more easily) by similar deoxymercuration of XI. The latter also yields, with sodium stannite, a mixture from which X may be isolated but the yield is lower, probably because of the presence of chloride ion.

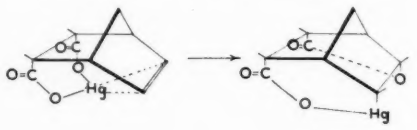
When XI is boiled with aqueous sodium hydroxide it is converted (evidently via lactone hydrolysis) by prototropic rearrangement into 5-↓-hydroxy-6-↓-chloromercuri-1,4-↑↑-methylenecyclohexane-2-↓-3-↑-dicarboxylic acid (XII). The alteration in the rearranged substance is proved by deoxymercuration to 1,4-↑↑-methylene-Δ^5-cyclohexene-2-↓-3-↑-dicarboxylic acid by means of hydrochloric acid. Further proof is obtained when XII is treated with sodium amalgam, which effects replacement of chloromercuri by hydrogen. The product (which shows no tendency toward spontaneous lactonization) evidently is 5-↓-hydroxy-1,4-↑↑-methylenecyclohexane-2-↓-3-↑-dicarboxylic acid.

The prototropic rearrangement of XI→ XII is replicated by the conversion X → XIV, although the absence of chloride ion is essential to the latter conversion. The chloride was precipitated as calomel. The 2-carboxyl group seems to be rearranged, since XIV is the lactone of what must be 5-↓-hydroxy-6-↑-chloromercuri-1,4-↑↑-methylenecyclohexane-2-↑-3-↓-dicarboxylic acid. Confirmation of this structure assignment follows deoxymercuration of XIV with concentrated hydrochloric acid, which yields 1,4-↑↑-methylene-Δ^5-cyclohexene-2,3-↓↑-dicarboxylic acid (XIII). Moreover, replacement of the chloromercuri group (with sodium amalgam) by hydrogen leads to the known 5-↓-hydroxy-1,4-↑↑-methylenecyclohexane-2-↑-3-↓-dicarboxylic acid, γ-lactone (19).

The oxymercurial from norbornene has been assigned the ↑↓ configuration and that from 1,4-↑↑-methylene-Δ^5-cyclohexene-2,3-↓↓-dicarboxylic acid (VII) the ↓↓ configuration (XI), yet both reactions seem to proceed by the same (ionic) mechanism. It might then be expected that a reaction would exist in which both ↓↓ and ↑↓ configurations would

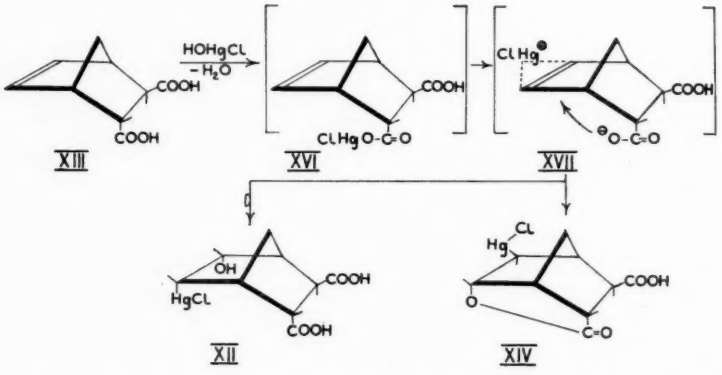
appear in the product. This expectation is realized in the treatment of 1,4-↑↑-methylene-Δ^5-cyclohexene-2,3-↑↓-dicarboxylic acid (XIII) with basic mercuric chloride in water, since both XII and XIV are obtained as products with the former predominating.

From these examples, it seems reasonable to assume that the norbornenes are oxymercurated uniquely via a π complex with mercuric salts which once was specified for alkenes in terms of an alkene–mercurinium ion (3). The favored neutralization of such an intermediate seems to occur from that region of the norbornane cage farthest from the methylene bridge. The mercuri group will then be situated in that region of the cage where the methylene bridge is predominant, unless it is attracted by an anionic group such as carboxyl in an available (↓) position. The simplest instance where both neutralizing anion and mercuri-attracting anion are two ↓↓ carboxyl groups is exemplified by the π-co-ordinated mercuric salt, XV, which is transformed to IX.



XV IX

When only one ↓ carboxyl group is available, as in 1,4-↑↑-methylene-Δ^5-cyclohexene-2-↓-3-↑-dicarboxylic acid (XIII), it seems to play either of the two roles alternatively. Thus it may neutralize the cation XVII formed via the intermediate XVI to yield XIV, or it may attract the mercuri group while hydroxyl ion is the neutralizing species, in which case XII is formed. One might expect in these circumstances that some of the 5-↑-OH diastereomer would be formed despite a preferential anionic approach to the cage. We have not found this diastereomer, but we cannot affirm its absence in view of the difficulties of separation. We shall now present evidence that such anionic neutralization does occur.

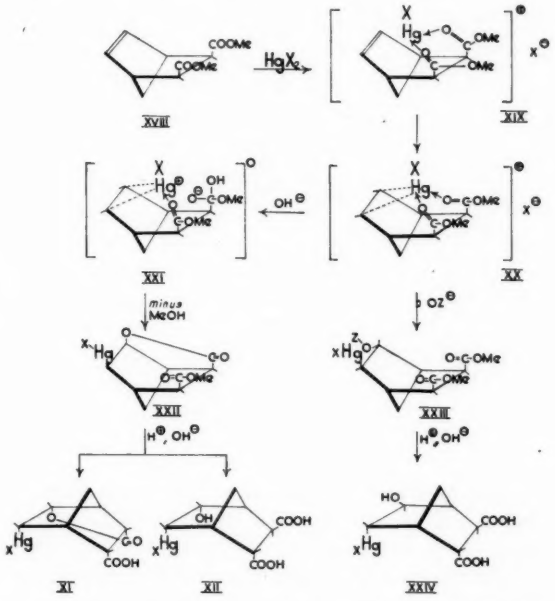


XIII XVI XVII XII XIV

This evidence is afforded by oxymercuration of dimethyl 1,4-↑↑-methylene-Δ^5-cyclohexene-2,3-↓↓-dicarboxylate (XVIII). Previously, the hydroxymercuration of this substance was reported (11) and the product was specified as 5-↓-hydroxy-6-↓-chloromercuri-2-↓-carbomethoxy-1,4-↑↑-methylenecyclohexane-3-↓-carboxylic acid, γ-lactone (XXII). It is now known that XXII from this reaction is contaminated with 5-↑-hydroxy-6-↓-

chloromercuri-2-↓-carbomethoxy-1,4-↑↑-methylenecyclohexane-3-↓-carboxylic acid, perhaps as its methyl ester, XXIII, though neither has been isolated. However, the presence of this mono- or di-ester impurity is shown by saponification of the entire product. The main product of this saponification is 5-↓-hydroxy-6-↓-chloromercuri-1,4-↑↑-methylenecyclohexane-2,3-↓↓-dicarboxylic acid, γ-lactone (XI), as well as some of the 2-↓-3-↑-dicarboxylic acid (XII) arising by prototropic rearrangement of XI. The remainder is isolated as 5-↑-hydroxy-6-↓-chloromercuri-1,4-↑↑-methylenecyclohexane-2-↓-3-↑-dicarboxylic acid (XXIV), the chemistry of which is discussed below. Thus the dimethyl ester of VII is shown to oxymercurate both ↓↓ and ↓↑, the former being predominant.

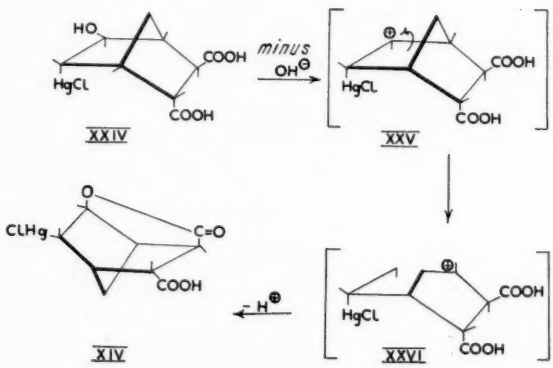
When dimethyl 1,4-↑↑-methylene-Δ^5-cyclohexene-2,3-↓↓-dicarboxylate (XVIII) is treated with mercuric acetate in acetic acid, the reaction is very rapid. The main product, almost pure, is dimethyl 5-↑-acetoxy-6-↓-chloromercuri-1,4-↑↑-methylenecyclohexane-2,3-↓↓-dicarboxylate (XXIII, Z = CH_3CO) plus a small quantity of 5-↓-hydroxy-6-↓-chloromercuri-2-↓-carbomethoxy-1,4-↑↑-methylenecyclohexane-3-↓-carboxylic acid, γ-lactone (XXII, X = Cl). When XXIII (Z = CH_3CO) is hydrolyzed, a prototropic rearrangement of one carboxyl group occurs to yield XXIV. This shift is indicated because



deoxymercuration of XXIV with hydrochloric acid yields 1,4-↑↑-methylene-Δ^5-cyclohexene-2-↓-3-↑-dicarboxylic acid (XIII). However, XXII (X = Cl), which may be prepared in excellent yield by mercuration of XVIII with an aqueous solution of mercuric acetate, and XXIII (Z = Me, X = Cl) prepared by methoxymercuration of XVIII, both deoxymercurate with hydrochloric acid to yield 5-↓-hydroxy-1,4-↑↑-methylenecyclohexane-2,3-↓↓-dicarboxylic acid, γ-lactone. Of course, this does not indicate which carboxyl group in XXIII has diastereomerically shifted. Indeed, XXIV could be either 5-↑-hydroxy-6-↓-chloromercuri-1,4-↑↑-methylenecyclohexane-2-↓-3-↑- or 2-↑-3-↓-dicarboxylic acid, but a pyrolytic reaction seems to supply this information.

The 5-↑-hydroxy-6-↓-chloromercuri-1,4-↑↑-methylenecyclohexane-2-↓-3-↑-dicarboxylic acid (XXIV) exists in two forms which evidently are polymorphs since the distortion polarizations and the infrared spectra (900–300 cm^{-1}) are practically identical although the melting points and X-ray diffraction patterns are different. The lower melting of these polymorphs tends slowly to resolidify slightly above its melting point of 194°. If it is maintained at 194–200° for 15 minutes the recognizable product is 5-↓-hydroxy-6-↑-chloromercuri-1,4-↑↑-methylenecyclohexane-2-↑-3-↓-dicarboxylic acid, γ-lactone (XIV). This inversion of the methylene bridge seems to be characteristic of the configuration of XXIV (since XII did not rearrange in this manner) and probably is a consequence of the 5-↑-hydroxy configuration. The rearrangement may be described in terms of the intermediates XXV and XXVI, and is typical of dehydration which otherwise would establish a bridgehead unsaturation.

In order to eliminate the possibility that the oxymercuration position assignments were incorrect, and that XXIV and XII differed only in the configuration of the chloromercuri group, the acid XXIV has been treated with sodium amalgam. The product has been designated as 5-↑-hydroxy-1,4-↑↑-methylenecyclohexane-2-↓-3-↑-dicarboxylic acid; certainly it is not identical with the acid of like composition which has been obtained by reduction of XII. It would seem that XXIV and XII differ in the configuration of the hydroxyl group.



The configurations of the oxymercurials derived from dimethyl 1,4-↑↑-methylene-Δ^5-cyclohexene-2,3-↓↓-dicarboxylate seem to be established and the mode of their formations may be suggested. The mechanism may be described essentially as was that of the corresponding acid. If the ester (XVIII) co-ordinates with mercuric acetate (X = OAc) a near-ionic form, XIX, may occur. Within the electropositive portion further co-ordination with the π bond (XX) will be a prelude to further reaction. If the reaction occurs in water, hydroxyl ion may be expected to perform the first step of an ester hydrolysis, i.e. to add to the carbomethoxyl group and form the externally neutral dipole, XXI. This internal mercurinium salt, by loss of methanol, would then culminate in the principal product, XXII. If some hydroxyl ion (or the ever-present acetate ion X) were to attack rearward of the mercurinium linkage (OH or OAc = OZ) then the product of inversion (XXIII) is expected and, in small amount, is obtained. In absence of the hydrolytic reaction, that is, when the reaction medium is acetic acid, XXIII, the product

of inversion, is obtained in 93% yield, and XXII in small amount (0.5%). This attack by acetate from the region of the cage where the methylene bridge predominates is contrary to that observed with norbornene. This opposite behavior is attributed in the present mechanism to the complexity of the ion, XX.

In connection with the ionic mechanism which has been postulated for the norbornenedicarboxylic acids and their derivatives it may be recalled that inclusion of boron fluoride etherate during the oxymercuration of norbornene largely excluded the acetoxy derivative, III, in favor of the methoxy derivative, IV (R = Me). This behavior is expected when acetate and methoxide ions are competing in an ionic process because of the preferential stabilization of methoxide ion by the Lewis acid, BF_3. It is of interest that the oxymercuration of the ester, XVIII, in methanol leads to XXIII in which Z is almost entirely aceto. However, a mixture is formed in which Z is partly methyl when boron fluoride is included with the methanol. Since the measured dipole moment of this methoxy derivative is of the same magnitude as that of XXIII (Z = CH_3CO), we presume that the configuration is identical. The mechanism of reaction thus seems to be the same as that postulated for oxymercuration of norbornene.

It will be noted in the preceding paragraph that configurational identity has been claimed on the basis of dipole moments. Also configurational relationships must be established between the mercurials from norbornenedicarboxylic acids (the configuration of which has been established by definitive physical and chemical criteria) and the mercurials from norbornene. Therefore the basis for the relationship according to the moment values of Table III must be established.

It must be understood that the moment values per se do not establish configurations but only relate known to unknown configurations. Moreover the moment values must only be considered of qualitative significance. Of course the actual values, all determined at 20° in dioxane (the only non-polar solvent in which all the mercurials are soluble), are reliable within 0.1 D. However, the vectorial assignments and the group moments must be chosen somewhat arbitrarily; indeed another set might have been chosen which would designate configurations opposite to those specified in this report. Nevertheless, like much physical interpretation based on factual logic and non-factual assumptions, the moment calculations are at least self-consistent. As such they suffice to relate the configurations assigned in this report.

Among the group moment assignments which must be made for the calculation is that of the chloromercuri group. A linear (20) and later an angular (21, 22) (+)C—Hg—Cl(−) has been proposed. The angularity must be revised anew in view of evidence (23) that the C—Hg moment is not negligible. Indeed, the measured polarizations of mercuracyclohexane and mercuracycloheptane (0.86 and 0.90 D respectively) show that the bond moment of C—Hg is 1.31 D, negative with respect to carbon, if the C—Hg—C angle is 140°. Then despite uncertainty of mercurial bond angles (23) one may assign to a typical mercurial, *n*-propylmercuric chloride (3.70 D), a C—Hg—Cl bond angle of about 80° if the Hg—Cl moment is 3.2 D. The latter value has been chosen in consideration of the increasing dipole moment of alkylmercuric halides with ascent of the homologous series (23). Essentially these assignments designate mercury as the positive end of the angular alkanemercuric chloride dipole.

A structural assignment must also be made for the gamma-lactone linkage. This assignment has not been made previously, perhaps because the reported values, 3.8 (24) to 4.1 D (25), for γ-butyrolactone are abnormally high by contrast with non-cyclic

TABLE III

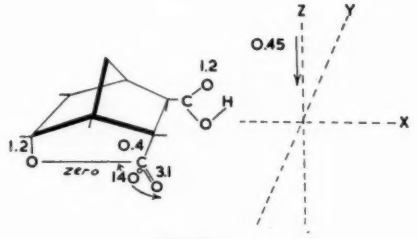
Electrical polarizations (cc) in dioxane at 20° C, moment in Debye units

	$\Delta\epsilon/\Delta\omega$	$\Delta\overline{V}/\Delta\omega$	P_T	$P_{\epsilon+a}$ pellet	R_D calc.	μ
5-↓-Hydroxy-2-carbomethoxy-1,4-↑↑-methylene-cyclohexane-3-↓-carboxylic acid, γ-lactone	15.53	0.165	542.9		45.1	4.86
1,4-↑↑-Methylene-Δ^5-cyclohexene-2,3-↓↑-dicarboxylic acid (XIII)	3.50	0.220	143.4		42.0	2.19
Same, except-2,3-↓↓-dicarboxylic acid (VII)	4.35	0.295	164.3		42.0	2.42
1,4-↑↑-Methylenecyclohexane-2,3-↓↓-dicarboxylic acid	5.50	0.230	204.8		42.4	2.78
1,4-↑↑-Methylenecyclohexane-2,3-↓↑-dicarboxylic acid	4.40	0.210	172.7		42.4	2.49
5-↓-Hydroxy-1,4-↑↑-methylenecyclohexane-2,3-↓↓-dicarboxylic acid, γ-lactone	16.70	0.265	535.1		40.4	4.85
5-↓-Hydroxy-1,4-↑↑-methylenecyclohexane-2-↑-3-↓-dicarboxylic acid, γ-lactone	18.30	0.275	578.8		40.4	5.06
Dimethyl 5-↑-acetoxy-6-↓-chloromercuri-1,4-↑↑-methylenecyclohexane-2,3-↓↓-dicarboxylate (XXIII, Z = CH_3CO, X = Cl)	6.30	0.545	579.5		78.9	4.87
Norcamphane (norbornane)	0.09	0.210	34.11		30.1	0.43
Norbornene (I)	0.28	0.185	35.6		29.7	0.53
5-↑-Methoxy-1,4-↑↑-methylenecyclohexane-2,3-↑↑-dicarboxylic acid	6.00	0.295	249.9		47.6	3.10
5-↑-Hydroxy-1,4-↑↑-methylenecyclohexane-2,3-↓↓-dicarboxylic acid	7.25	0.612	557.5	88.9	60.2	4.73
dd,ll-2,2'-↑↑-Mercuri-bis-3-↓-methoxy-1,4-↑↑-methylenecyclohexane, m.p. 68° (V, *dd,ll*)	1.0417	−0.36364	156.8	81.1	81.8	1.93
dl,ld of same, m.p. 108° (V, *dl,ld*)	1.250	−0.3333	176.2	81.4	81.8	2.17
3-↓-Methoxy-1,4-↑↑-methylenecyclohexyl-2-↑-mercuric chloride (IV, R = Me, X = Cl)	6.250	−0.4500	427.5		52.4	4.22
3-↓-Methoxy-1,4-↑↑-methylenecyclohexyl-2-↓-mercuric chloride (VI)	2.857	−0.555	214.2		52.4	2.77
3-↓-Acetoxy-1,4-↑↑-methylenecyclohexyl-2-↑-mercuric chloride (III)	4.40	0.505	329.8		57.1	3.60
5-↓-Hydroxy-6-↓-chloromercuri-1,4-↑↑-methylene-cyclohexane-2-↓-3-↑-dicarboxylic acid (XII)	5.33	0.605	405.6		56.4	4.07
5-↓-Hydroxy-6-↑-chloromercuri-1,4-↑↑-methylene-cyclohexane-2-↑-3-↓-dicarboxylic acid, γ-lactone (XIV)	9.90	0.610	716.1		56.4	6.40
5-↓-Hydroxy-6-↑-chloromercuri-1,4-↑↑-methylene-cyclohexane-2,3-↓↓-dicarboxylic acid, γ-lactone (X)	16.10	0.585	1143.4		56.4	7.18
Same, except -6-↓-chloromercuri- (XI)	4.85	0.600	373.0		56.4	3.88
5-↓-Hydroxy-6-↓-chloromercuri-2-↓-carbomethoxy-1,4-↑↑-cyclohexane-3-↓-carboxylic acid, γ-lactone (XXII)	4.50	0.545	366.6		61.1	3.81
Dimethyl 5-↑-methoxy-6-↓-chloromercuri-1,4-↑↑-methylenecyclohexane-2,3-↓↓-dicarboxylate (XXIII, Z = Me, X = Cl)	5.80	0.537	508.2		74.2	4.54

little-constrained esters. It seems reasonable to explain this high value as an alteration of bond moments in the —C—O—(C=O)—C linkage from [0.7, 0.7, 2.3, 0.4] to [0.8, 0.5, 2.8, 0.4], after which the moment for γ-butyrolactone is calculated as 4.0 D.

However, the moments of the 5-↓-hydroxy-1,4-↑↑-methylenecyclohexane-2,3-↓↓-dicarboxylic acid, γ-lactone (μ = 4.85 D), and the 2,3-↑↓-diastereomer (μ = 5.06 D) markedly exceed that of γ-butyrolactone. Part of this abnormality may be ascribed to the norbornane ring since a moment of 0.43 D has been observed (Table III) for this hydro-

carbon. The carboxyl group will also contribute, but neither contribution suffices to explain the high moment which has been observed, especially for the 2,3-↑↓-diastereomer. However, it is probable that the additional constraint imposed by the norbornane cage accentuates the alteration in bond moment which has been suggested for γ-butyrolactone.



XXVII

These considerations have suggested the model XXVII in which the alcohol bond is extended to 1.2 D and the carbonyl bond is extended to 3.1 D, while the ester bond is decreased to zero. This condition represents a resonance hybridization of the O—C═O linkage. Moreover the constraint imposed by non-planarity of the γ-lactone ring has distorted the cyclohexane ring so that the ↓ linkages are inclined 18° toward the center of the cage, thus forcing the equatorial ↑ linkage into a plane containing atom 2, 3, 5, and 6. These linkages are assumed to be spread 30° outward from the *X*-axis.

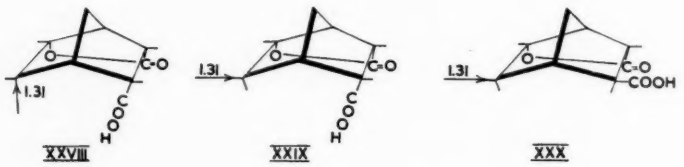
The moment of the free carboxyl group has been estimated as 1.2 D by calculation from the observed moments of 1,4-↑↑-methylenecyclohexane-2,3-↓↓-dicarboxylic acid (μ = 2.78 D) and 1,4-↑↑-methylenecyclohexane-2,3-↑↓-dicarboxylic acid (μ = 2.49 D) after subtraction of the norbornane cage moment (0.45 D). In order to simplify subsequent calculations the moment of the carboxyl groups (either ↑ or ↓) has been assumed to be symmetrical about the C—COOH bond. That is to say that the hydroxyl group in the carboxyl is in *cis* relationship to the carbonyl group.

In these circumstances the moment summation with respect to the co-ordinate axes is found to be 4.86 D for 5-↓-hydroxy-1,4-↑↑-methylenecyclohexane-2,3-↓↓-dicarboxylic acid, γ-lactone, and 5.04 D for the 2,3-↑↓-diastereomer. If the C—Hg group moment assigned previously (1.31 D, C ← Hg) is added to each of these γ-lactones in the appropriate sense the following R—Hg moments arise from the calculation.

Calculation of the moment of 5-↓-hydroxy-6-↓-chloromercuri-1,4-↑↑-methylenecyclohexane-2,3-↓↓-dicarboxylic acid, γ-lactone, from XXVIII may be made as follows:

$$\mu = [(3.79)^2+(3.22)^2-2(3.79)(3.22)\cos 41^\circ \cos 13^\circ \sin 10^\circ]^{\frac{1}{2}} = 4.6 \text{ D.}$$

It is not surprising that this value, based on harmonic rotation at a rate exceeding 500 kc/second, is appreciably higher than the observed moment (3.88 D) since free rotation



$\mu_{R\text{-}Hg}$ = 3.79 D where $\tan\mu_Y/\mu_Z = \tan 11°$ and $\tan\mu_X/\mu_Z = \tan 43°$

$\mu_{R\text{-}Hg}$ = 5.87 D where $\tan\mu_Y/\mu_X = \tan 23°$ and $\tan\mu_Z/\mu_X = \tan 43°$

$\mu_{R\text{-}Hg}$ = 6.31 D where $\tan\mu_Y/\mu_X = \tan 18°$ and $\tan\mu_Z/\mu_X = \tan 27°$

would be most improbable. Calculation at position 6 for the quadrant directions of Hg → Cl shows that when this vector points toward the 2-position the moment would be 6.2 D; away from position 2, 2.3 D; toward position 5, 5.0 D; and away from position 5, 4.3 D. Therefore the observed moment is about what would be expected if rotation were hindered within the realm of the norbornane cage, thus minimizing the 6.2 D and the 5.0 D conformations.

The moment calculation from XXIX for 5-↓-hydroxy-6-↑-chloromercuri-1,4-↑↑-methylenecyclohexane-2,3-↓↓-dicarboxylic acid, γ-lactone (X), assuming free rotation, is 7.0 D. While this is lower than the observed moment (7.18 D) the slight discrepancy is not unexpected in view of possible hindrance when Hg → Cl is directed toward C_5. This conformation detracts slightly from the total because of the angle of 120° which the Hg—C bond makes with the C_5—C_6 bond. Consequently, the observed moment may be expected to be slightly higher than that calculated for harmonic free rotation.

However, a greater discrepancy exists between observed moment (6.4 D) and that calculated (7.50 D) from the partial structure, XXX, for 5-↓-hydroxy-6-↑-chloromercuri-1,4-↑↑-methylenecyclohexane-2-↑-3-↓-dicarboxylic acid, γ-lactone (XIV). Several explanations are possible to account for this discrepancy. First, the assumption that the carboxyl group is bound so that its group moment is linear may apply to the ↓ position where it is "bound" by the lactone resonance but not to the ↑ (actually equatorial) position. Thus it may contribute, together with the chloromercuri group, three rotators in the structure. The equation for a single rotator would then not apply. More likely is the possibility that this heavy molecule exists as a carboxylic acid dimer which is stable even in very dilute solution because of the non-hindered equatorial carboxyl group. This hydrogen-bridging would effectively lower the moment. Some evidence for this bridging is found in the fact that the moment in dioxane increases from 6.40 D at 25° to about 6.6 D at 70°.

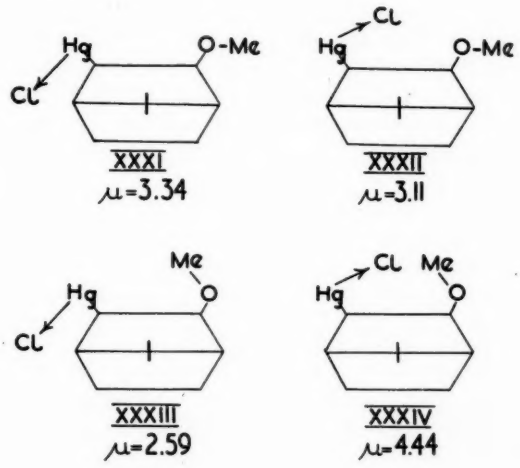
However, it is advisable to consider only qualitatively any moment value in which more than two rotators are involved. For this reason there are numerous entries in Table III for which no calculations are attempted. However, a typical example may be chosen in the observed moment of 3-↓-acetoxy-1,4-↑↑-methylenecyclohexyl-2-↑-mercuric chloride (3.6 D, III). When the accepted value (1.80 D) for the acetoxy group (26) in its *cis* conformation is used with a calculated moment angle of 121° the over-all molecular moment where two rotators are inclined at 120° is 4.0 D. However, the discrepancy may be made to disappear and then to reappear in a moment value lower than that observed by alteration in the rotations at the ether linkage and the carbonyl linkage in the acetoxy

group. Since the anharmonicity of these rotators is unknown, the calculation is of little significance.

The moment calculation for 3-↓-methoxy-1,4-↑↑-methylenecyclohexyl-2-↑-mercuric chloride (IV) is more propitious because only two rotators are involved. The rotation is assumed to be harmonic. One rotator is C—Hg—Cl with a group moment of 3.67 D and moment angle 79° from C—Hg. The other rotator is a combined norbornane plus methoxyl moment ($\mu_g = 1.30+0.43 \cos 55° = 1.59$ D). The rotator axes are separated by 65°. The resultant is 4.12 D, slightly low by comparison with the observed moment of 4.22 D. This discrepancy may be attributed to anharmonicity such as was postulated for the 2,3-↓↓-dicarboxy analogue (X) because of slight steric hindrance.

When μ for 3-↓-methoxy-1,4-↑↑-methylenecyclohexyl-2-↓-mercuric chloride (VI) is calculated on the same free-rotatory basis as is the diastereomer, IV, the value, 3.4 D, is considerably higher than has been measured (2.88 D). However, a consideration of the quadrant conformations shows that XXXIV surely is excluded on the basis of hindrance between chloromercuri and methoxy. Probably XXXII is excluded for the same reason. The average calculated moment due to XXXI and XXXIII is 2.86 D, in agreement with the observed value.

The reasonable adjustments which have been made in calculation are required to bring the norbornane oxymercurials of unknown configuration into correlation with the known configuration of the norbornane dicarboxylic acid mercurials. However, these adjustments have a further significance because those diastereomers (↓↓) in which hindrance is assumed to exist are also the ones which are most easily deoxymercurated.



The mechanism of deoxymercuration has been suggested variously as due to polar (27) and steric effects (28), and both probably are operative. Certainly the extreme resistance of alkylmercuric halides and the moderate resistance of arylmercuric halides toward demercuration, in contrast to comparatively easy deoxymercuration, shows that polarity of substituents is significant. The static aspects of steric effect have been shown by experiment to be profound. Additionally, and related both to polarity and geometry, are the internal degrees of freedom. The acceptance of the deoxymercurating agent either

by co-ordination with the oxy group (polar mechanism) or in concerted cyclic transition states (steric (28)) must be related to molecular flexibility. The rigidity imparted by the norbornane cage makes it possible to correlate the moment values with the ease of deoxymercuration and thus to justify the behavior of 5-↓-hydroxy-6-↓-chloromercuri-1,4-↑↑-methylenecyclohexane-2,3-↓↓-dicarboxylic acid, γ-lactone (XI), and the simpler mercurial, VI, which is configurationally related to it.

In summary, the calculations show that since the dipole moment of 5-↓-hydroxy-6-↓-chloromercuri-1,4-↑↑-methylenecyclohexane-2,3-↓↓-dicarboxylic acid, γ-lactone (XI, the configuration of which is known), is lower than that of 5-↓-hydroxy-6-↑-chloromercuri-1,4-↑↑-methyleneeyclohexane-2,3-↓↓-dicarboxylic acid, γ-lactone (X), the moment of the norbornene methoxymercurial (which is higher than that of the diastereomer to which it may be rearranged) designates it as 3-↓-methoxy-1,4-↑↑-methylenecyclohexyl-2-↑-mercuric chloride. The addition of the elements of methoxymercuric salts to norbornene thus occurs in the ↓↑ (so-called *trans*) manner. In part, this is true for oxymercuration of all norbornenes except 1,4-↑↑-methylene-Δ^5-cyclohexene-2,3-↓↓-dicarboxylic acid (VII). The oxymercuration of all norbornenes seems to be acid-catalyzed. This catalysis as well as the ultimate configuration indicates that oxymercuration of norbornenes occurs by an ionic mechanism which may be expressed in terms of a cationic intermediate such as the alkene–mercurinium ion postulated by Lucas, Hepner, and Winstein (3).

But the oxymercuration of cyclohexene, for which this postulate was made, is neither acid-catalyzed nor does the product resemble the oxymercurial from norbornene in respect of moment magnitude and resistance toward deoxymercuration. The same dissimilarity applies to the oxymercurials of cyclopentene, α-terpineol, and also of the stilbenes if conformational aspects are taken into consideration. Although the postulation of Lucas, Hepner, and Winstein seems to apply to a bicyclic alkene in which electron field distortion is probable, this postulation is unrealistic in respect of the conformationally restricted type of alkene for which it was promulgated. The latter type seems to be oxymercurated by a molecular mechanism which causes ↓↓ (so-called *cis*) addition. However, ↑↓ oxymercuration might be found to occur among α,β-unsaturated carbonyl compounds.

The authors wish to thank the National Research Council for funds in support of this research, and also Dr. Henry Richmond for aid in some of the moment calculations.

EXPERIMENTAL

Physical Constants

Melting points have been corrected against reliable standards (29). X-Ray diffraction patterns have been made with Cu K_α (Ni-filtered) radiation and are expressed as relative intensities $[I/I_1]$ for d spacings in Å. Temperature composition diagrams have been determined (1° per minute) by the method of Rheinboldt and Kirscheim (30). Electrical polarizations in dioxane solutions were made with the apparatus and method described previously (31), and no value of $\Delta\epsilon/\omega_2$ or $\Delta\bar{V}/\omega_2$ was accepted unless the extrapolation matched the ϵ and $\bar{V}$ for pure dioxane. Distortion polarizations were determined from compressed pellets and/or additive group refractions.

Purification of Reagents

The norbornene (1,4-↑↑-methylene-Δ^2-cyclohexene, 100 g) was shaken twice at 50° with 200 ml of 5% aqueous ferrous sulphate in a separatory funnel under nitrogen, then twice with 50-ml portions of water. After it was dried under nitrogen with magnesium sulphate the norbornene was distilled under nitrogen at 95–97°, then fractionated under

nitrogen in a 100-plate column, reflux ratio 1:35, b.p. 97–98°, m.p. 45–47°. The mercuric acetate was crystallized from acetic acid (2.5 ml per g) and was washed with anhydrous ether until the odor of acetic acid no longer could be detected.

3-↓-Hydroxy-1,4-↑↑-methylenecyclohexyl-2-↑-mercuric Chloride (IV, R = H, X = Cl)

A system consisting of 0.94 g (0.01 mole) of norbornene with 3.18 g (0.01 mole) of mercuric acetate and 0.2 ml of concentrated nitric acid in 35 ml of water was allowed to react 1 day and then was treated with aqueous sodium chloride. The product (88%) melted at 124–128° and was purified for analysis (see Table IV) by crystallization from 1:1 ethanol–water. When the nitric acid was not included the crude melting point was 119–125° and treatment with alkali was required to saponify the acetate which was present as an impurity. The other derivatives of Table IV were prepared by treatment with the appropriate sodium halide.

3-↓-Acetoxy-1,4-↑↑-methylenecyclohexyl-2-↑-mercuric Acetate (III, X = OAc)

To 6.36 g (0.02 mole) of mercuric acetate suspended in 30 ml of 2,5-dioxahexane was added 1.88 g (0.02 mole) of norbornene. After 5.5 hours the insoluble substance was filtered off and washed with 30 ml of dioxahexane, 6.55 g (79%), m.p. 98–100°. The substance was obtained in 84% yield by use of acetic anhydride as the reaction medium (32). Calc. for $C_{11}H_{16}HgO_4$: Hg, 48.7. Found: Hg, 49.3.

4-↓-Acetoxy-1,4-↑↑-methylenecyclohexyl-2-↑-mercuric Chloride (III, X = Cl)

(*a*) *By Acetylation*

To 2 ml of anhydrous pyridine was added 0.5 g (0.0014 mole) of 3-↓-hydroxy-1,4-↑↑-methylenecyclohexyl-2-↑-mercuric chloride. To this solution was added 1 ml (0.0065 mole) of acetic anhydride. After 2 days at room temperature the system was poured into 20 ml of cold 5% aqueous sodium chloride. The slowly solidifying product (0.56 g, 98%) melted at 122–124°. After two crystallizations from acetone the melting point (130°) of the product was not depressed by a sample prepared according to procedure (*b*). The substance was found by flotation in thallium formate – malonate at 5° to have a density of 2.37.

(*b*) *By Salt Exchange*

The compound may be obtained in 8% yield by dilution of the mother liquors from the acetate (see above) with aqueous sodium chloride. Alternatively, 1.04 g (0.0025 mole) of 3-↓-acetoxy-1,4-↑↑-methylenecyclohexyl-2-↑-mercuric acetate was shaken with 25 ml of 5% aqueous sodium chloride for 2 hours, converting it to 0.87 g (88%) of the chloromercurial, m.p. 124–128°. Crystallization from acetone (7 ml per g) raised this melting point to 130.8–131.8° (0.63 g).

The X-ray diffraction pattern was determined: [10] 14.40; [7] 4.77, 4.27, 3.86, 3.53, 2.79; [6] 5.71, 2.41; [5] 5.27, 3.12, 2.47; [4] 8.58, 5.90, 4.00, 3.62, 3.06, 2.98, 2.90, 2.51, 2.25; [3] 3.41, 3.25, 2.66, 2.62, 2.35, 2.31, 2.14; [2] 4.13, 2.19, 2.10, 1.96, 1.93, 1.86, 1.81, 1.77; [1] 7.02, 3.34, 2.27, 2.06, 2.00, 1.72, 1.64, 1.36, 1.24, 1.34; [0.5] 4.95, 2.85. Calc. for $C_9H_{13}ClHgO_2$: C, 27.8; H, 3.34; Hg, 51.6. Found: C, 28.0; H, 3.47; Hg, 52.0.

(*c*) *From Norbornene*

To 5 ml of anhydrous peroxide-free 2,5-dioxahexane was added 0.4 g (0.0017 mole) of mercuric acetate with or without a catalyst. To this suspension was added 0.11 g (0.0017 mole) of norbornene and the system was agitated for 4.5 hours, then filtered into 15 ml of 5% aqueous sodium chloride. After 1.5 hours, filtration with water-washing gave 0.65 g (98%), m.p. 126–128°, when no catalyst was added. Addition of boron fluoride

etherate depressed the melting point but not the yield. Addition of 0.00017 mole of pyridine depressed both (62%, m.p. 122–155°) while 0.0017 mole of this retarder depressed both to 24%, m.p. 121–125°. Under the latter conditions a prolonged reaction time (11 hours) increased this low yield to 41%, m.p. 122–124°. The catalytic effect of an equivalent of methanol was found to be negative since a yield of 70%, m.p. 120–125°, was obtained. None of these products gave a melting point depression upon admixture with the purified product of procedures (*a*) and (*b*). Reaction in glacial acetic acid (15 ml) was more rapid than in dioxahexane. The clear solution, after 30 minutes, was drowned in 30 ml of 5% aqueous sodium chloride giving a quantitative yield, m.p. 127–129°. Two crystallizations from acetone (6 ml per g) raised this melting point to 130°.

3-↓-Methoxy-1,4-↑↑-methylenecyclohexyl-2-↑-mercuric Chloride (IV, R = Me, X = Cl)

(*a*) *By Methylation*

From a 250-ml claisen flask containing 80 ml of sulphur-free toluene was distilled 15 ml to remove water. Then 0.59 g (0.015 atom) of potassium and 10 ml of sodium-dried *tert*-butyl alcohol was added. When solution was complete the excess of *tert*-butyl alcohol was distilled off. Then 1.8 g (0.005 mole) of 3-↓-hydroxy-1,4-↑↑-methylenecyclohexyl-2-↑-mercuric chloride was dissolved in the stirred system. After 90 minutes the whole was partially vacuum-distilled to remove *tert*-butyl alcohol. To the remainder was added 1.89 g (0.015 mole) of pure dimethyl sulphate. After the solution was stirred for 90 minutes 40 ml of 10% aqueous sodium hydroxide was added. The remaining toluene was vacuum-distilled off after 15 minutes. The residue, diluted with 90 ml of 1.5% aqueous sodium chloride, was treated exhaustively with gaseous carbon dioxide. The precipitate, 1.4 g (77%), m.p. 119–122°, was crystallized from absolute ethanol, m.p. 121–123°. A mixture melting point with the methoxymercurial prepared according to procedure (*b*) or by Rowland's procedure (8) was not lowered. The density, determined by flotation at 5° in an aqueous thallium formate – malonate solution, was 2.41. Oxidation with alkaline permanganate was difficult and much unchanged mercurial was recovered. However, a 10% yield of 1,3-↓↓-cyclopentanedicarboxylic acid, m.p. 119°, was obtained.

(*b*) *By Standard Oxymercuration*

To 10 ml of absolute methanol containing the catalyst (see Table II) was added 0.23 g (0.0025 mole) of norbornene. To the homogeneous solution was added with shaking 0.80 g (0.0025 mole) of mercuric acetate. The homogeneous reaction continued for 90 minutes; then the system was chilled to 5° and this temperature was maintained while 20 ml of 5% aqueous sodium chloride was added. The system kept at 5° during 2 hours was filtered, washed with water, and vacuum-dried. The typical yield with 0.5 equivalent of boron fluoride was 0.85 g (95%), m.p. 115–118°, or with 0.2 equivalent of ferrous sulphate was 95%, m.p. 108–114°. The product was analyzed as described below or was crystallized from hot carbon tetrachloride (1 ml per g), m.p. 120–121°. Melting point ranges were determined in the Rheinboldt apparatus, the temperature–composition diagram having been determined from known mixtures of methoxy- and acetoxy-mercurials which were together dissolved in chloroform and evaporated. The acetyl content of the known mixtures and the products were determined by the method of Friedrich (33).

(*c*) *From Mercuric Chloride*

A mixture of 0.94 g (0.01 mole) of norbornene and 2.71 g (0.01 mole) of mercuric chloride in 25 ml of methanol was maintained for 10 hours and then chilled to −60° and filtered to remove 0.67 g, m.p. 89.5–91.5°, which contained 0.30 g of benzene-insoluble mercuric chloride. The filtrate was diluted to a volume of 45 ml and was filtered quickly, 0.49 g,

m.p. 121–122°. The total yield (0.86 g, 24%) was crystallized from 2:1 hexane–benzene, m.p. 122–123°. A mixture melting point with the pure products of procedures (*a*) and (*b*) was not lowered.

(*d*) *By Mercuric Acetate plus Mercuric Oxide*

Suspensions of 10 ml of absolute methanol, 0.80 g (0.0025 mole) of mercuric acetate, and 0.10 g (0.0005 mole) of alkali-free yellow mercuric oxide were stirred under reflux in nitrogen for 8 hours. Each was then stirred for various periods of time after 0.23 g (0.0025 mole) of norbornene was added, then was chilled and treated with 20 ml of 5% aqueous sodium chloride and chilled to 5° overnight. The yield after 15 minutes and also after 4 hours was 70%, m.p. 92–101°, but after 12 hours it was 90%, m.p. 92–106°, indicating a retarded formation of methoxymercurial. The marked acceleration after 4 hours undoubtedly is related to the disappearance of suspended material after this time interval.

TABLE IV

Preparation and properties of 2-↓-alkoxy-1,4-↑↑-methylenecyclohexyl-2-↑-mercuric halides (IV) from equimolar amounts of norbornene (I) and mercuric acetate in the protonic medium (ROH), then treated with alkali halides (MX)

Properties	R = H X = Cl	R = H X = Br	R = H X = I	R = Me X = Cl	R = Me X = Br	R = Et X = Cl	R = Et X = Br
Yield	88	90	93	91	97	78	93
M.p., °C	128.6–129.3	130.7–131.2	146.6–147.2	123.0–123.7	89.3–89.8	64–65	80.4–81.2
% C:							
calc.	24.2	21.4	19.2	26.6	23.7	28.8	25.8
found	24.5	21.3	19.1	26.7	23.5	28.6	25.2
% H:							
calc.	3.20	2.81	2.52	3.63	3.20	4.01	3.58
found	3.62	2.99	2.57	3.77	3.40	4.17	3.44
% Hg:							
calc.	57.8			55.6		53.6	
found	57.6			56.2		53.5	
X-ray diagram							
[10]	8.63			9.50		13.80	
[9]	4.78			6.06		3.65	
[8]	5.12			5.12		5.57	
	3.31			4.95		4.55	
	3.51			3.56		3.42	
[7]	2.92			2.93		8.50	
	2.58			3.70		5.61	
	3.08			3.93		5.34	
[6]	2.80			3.35		4.30	
	2.54			3.06		4.20	
[5]	2.45			3.48		6.94	
	2.15			2.62		6.53	
	2.03			2.51		5.05	
	1.98			2.24		4.10	

2,2′-↑↑-Mercuri-bis-3-↓-methoxy-1,4-↑↑-methylenecyclohexane (V, *dd,ll and* V, *dl,ld*)

To 100 ml of 85% hydrazine hydrate chilled to −70° was added 27 g (0.0075 mole) of 3-↓-methoxy-1,4-↑↑-methylenecyclohexyl-2-↑-mercuric chloride. The temperature was allowed to rise slowly to that of the ice bath into which the system was transferred. After 20 minutes a pink color was observed which changed to blue-black. After 12 hours at 25° the whole was heated on the steam bath for 3 hours, then chilled for 12 hours.

The aqueous layer and the metallic mercury were decanted from the white solid (12 g, 70%, m.p. 70–110°) which was heated with 100 ml more of hydrazine hydrate on the steam bath for 11 hours. Chilling yielded 4.3 g (25%) of crude product, m.p. 62–66°, softening at 55°. The same color change and the same yield, but with lower melting point (56.2–57.5°), may be obtained if 1 mole of mercurial in 5 moles of 2.5% aqueous alkali is treated with 0.5 mole of stannous chloride dihydrate during 24 hours.

This mixture of two diastereomers may be separated by 'triangular' crystallization utilizing methanol in which the higher melting isomer is relatively insoluble and methanol–water from which the lower melting isomer may be crystallized. Finally the higher melting isomer was crystallized from acetone, m.p. 107.5–108°. The lower melting isomer finally was crystallized from methanol, m.p. 66–66.5°. The ratio of high to low was found to be 6 to 1. Calc. for $C_{16}H_{26}O_2Hg$: C, 42.7; H, 5.76. Found (high): C, 42.8; H, 5.73. Found (low): C, 42.7; H, 5.67. The X-ray pattern for the high melting diastereomer was [10] 10.64, 10.00, 5.82, 5.60; [6] 4.21, 3.87, 3.77, 3.47, 3.26; [4] 2.74, 2.65, 2.22, while that of the low melting isomer was [10] 11.33, 5.34, 4.79; [9] 7.76, 7.53, 3.90; [8] 3.61, 3.46; [6] 3.09, 3.02, 2.68, 2.59, 2.36, 2.40; [3] 2.15, 2.10.

When either the high or low melting isomer was refluxed for 3 hours with 2 equivalents of mercuric acetate in methanol, and then was treated with sodium chloride, the crude chloromercurials melted at 120–122°. A mixture melting point with 3-↓-methoxy-1,4-↑↑-methylenecyclohexyl-2-↑-mercuric chloride was not lowered. In each instance about 10% of bis-mercurial was recovered unchanged. The same chloromercurial, m.p. 121–122°, was obtained when either isomer was treated with methanolic hydrochloric acid for 5 minutes. Either isomer could be heated to 115° for 40 minutes without change.

An unsuccessful attempt was made to synthesize the bis-mercuri diastereomers by converting 0.9 g (0.0025 mole) of 3-↓-methoxy-1,4-↑↑-methylenecyclohexyl-2-↑-mercuric chloride either to the organomercuric acetate by 0.41 g of silver acetate or to the organomercuric hydroxide by treatment with silver oxide, both in methanol, followed by treatment with norbornene (0.47 g, 0.005 mole) and 12 mg of boron fluoride etherate. After 1 day the original mercurials were recovered unchanged.

1,4-↑↑-Methylenecyclohexan-↓-yl Phenylurethane

To 1.40 g (0.004 mole) of 3-↓-hydroxy-1,4-↑↑-methylenecyclohexyl-2-↑-mercuric chloride in 18 ml of methanol was added a solution of 0.32 g (0.008 mole) of sodium hydroxide in 1 ml of distilled water. This solution was refluxed 6 hours with 0.47 ml (0.008 mole) of 85% hydrazine hydrate; 0.70 g (87%) of the mercury was filtered off as the metal.

The filtrate, diluted with 75 ml of water, was ethyl ether-extracted (75 ml) and the extract was evaporated to 5 ml. The solid which crystallized, m.p. 151–152°, 0.28 g (62%), was 2-hydroxy-1,4-↑↑-methylenecyclohexane (no mercury). A mixture melting point with an authentic sample of 2-↓-hydroxy-1,4-↑↑-methylenecyclohexane (34) gave no depression. A 0.01-g (0.0009 mole) portion of the alcohol was treated with 1 equivalent of phenyl isocyanate in 3 ml of hexane for 1 day. The urethane, 0.15 g (60%), melted at 158–159° before and 160–161° after crystallization from benzene, mixture melting point not lowered.

3-↓-Methoxy-1,4-↑↑-methylenecyclohexyl-2-↓-mercuric Chloride (VI)

To 25.2 g (0.07 mole) of 3-↓-methoxy-1,4-↑↑-methylenecyclohexyl-2-↑-mercuric chloride (IV, R = Me, X = Cl) in 750 ml of water plus 5.60 g (0.14 mole) of sodium hydroxide was added 0.3 g of 100% hydrazine hydrate. After 6 hours the cooled system was ether-

extracted (30 ml) and the aqueous, metallic, and non-aqueous phases were separated. The aqueous phase was acidified with acetic acid to yield a variable amount of original mercurial admixed with bis-mercurial and product, m.p. 78–95°, mixture melting point with original mercurial 80–110°, maximum amount 12.1 g (48%).

The non-aqueous phase was evaporated leaving an oil, 4.80 g, which was dissolved in 35 ml of hot methanol. Then 2 ml of concentrated hydrochloric acid was added to the slightly warm solution. After 30 minutes at room temperature water was added to turbidity. The system was extracted by chloroform and this extract was vacuum-evaporated leaving 1.80 g of semisolid which was crystallized from carbon tetrachloride (11 ml per g), 1.5 g, m.p. 113–114°, 6% yield. Crystallization from absolute ethanol (30 ml per g) raised this melting point to 117.7–118.5°, recovery 45%. A mixture melting point with the original mercurial was lowered to 80–85°. Diffraction pattern: [10] 11.62; [8] 5.14, 4.14, 3.37, 3.14; [6] 6.91, 6.28, 5.21; [5] 3.09; [4] 3.87, 3.46, 2.15, 2.10. Calc. for $C_6H_{13}ClHgO$: C, 26.6; H, 3.63; Hg, 55.6. Found: C, 26.7; H, 3.74; Hg, 55.0.

In a variation the concentrate from the non-aqueous extract of the reaction system was shaken for 15 minutes with 150 ml of 10% hydrochloric acid. The gummy solid was dissolved in 125 ml of absolute ethanol, and 2 ml of 5% aqueous sodium chloride was added. After 30 minutes a precipitate appeared (m.p. 110–112°, yield 12%), which was purified to m.p. 117.5–118.5° as described above.

A mixture of this ↓↓-diastereomer and the ↑↓-diastereomer from which it was formed (0.1 g of each in 10 ml of methanol) was treated with 0.2 ml of hydrochloric acid for 40 minutes. Addition of sodium hydroxide precipitated mercuric oxide which was filtered off. The filtrate, upon acidification with acetic acid, precipitated 0.06 g (30%), m.p. 112–117°. Crystallization from absolute ethanol raised this melting point to 120–122°. A mixture melting point with the ↓↓-diastereomer was lowered to 95° while no depression was observed upon admixture with the ↑↓-diastereomer.

2-↓-Methoxy-1,4-↑↑-methylenecyclohexane

A suspension of 11 g (0.03 mole) of 3-↓-methoxy-1,4-↑↑-methylenecyclohexyl-2-↑-mercuric chloride in 50 ml of water was shaken slowly and 100 g (0.1 atom) of 2% sodium amalgam was added. After 12 hours the system was steam-distilled and the non-aqueous phase of the distillate was dried with magnesium sulphate and distilled, b.p. 59–62°, at 30 mm, 1.90 g (50%), n_D^{20} 1.4574. It was redistilled, b.p. 154–155°, at 750 mm, n_D^{20} 1.4572. This product could not be frozen at −80° C. The same product was obtained by reduction of 3-↓-methoxy-1,4-↑↑-methylenecyclohexyl-2-↑-mercuric chloride with an excess of hydrazine hydrate and by methylation of 2-↓-hydroxy-1,4-↑↑-methylenecyclohexane in diethyl ether by use of sodamide and methyl iodide. Calc. for $C_8H_{14}O$: C, 76.1; H, 11.25; OCH_3, 24.6. Found: C, 76.1; H, 11.17; OCH_3, 25.1.

5-↓-Hydroxy-6-↓-chloromercuri-1,4-↑↑-methylenecyclohexane-2,3-↓↓-dicarboxylic Acid, γ-Lactone, μ = 3.88 D (XI)

A solution of 1.82 g (0.01 mole) of 1,4-↑↑-methylene-Δ^5-cyclohexene-2,3-↓↓-dicarboxylic acid in 50 ml of water at 80° was agitated while 2.70 g (0.01 mole) of mercuric chloride dissolved rapidly. The product appeared within 6 seconds and was filtered off when the system was cool, m.p. 202°, 3.97 g (95%). By crystallization via solution in dimethylformamide and gradual precipitation with chloroform (the first slight precipitate being discarded) it melted at 225–226° when inserted about 10° below this melting point. The X-ray diffraction pattern was [10] 4.55; [9] 4.74; [8] 4.00; [7] 6.13, 6.57, 7.25; [5] 2.78; [4] 3.50; [3] 2.57; [2] 2.88, 2.98; [1] 5.51, 3.06; [0.5] 4.16, 3.43.

A repetition of this experiment in which 2 ml (0.02 mole) of concentrated hydrochloric acid was included showed that the reaction was retarded both with respect to time of appearance of product and disappearance of inorganic mercury. However, the ultimate yield was 2.68 g (89%). The delay was still longer (20 minutes) before the first precipitate appeared when 4 ml (0.04 mole) of hydrochloric acid was included and the final yield after 1 day was 75%. Conversely the inclusion of 4 ml (0.01 mole) of 10% aqueous sodium hydroxide in the system reduced the time for appearance of product to 3 seconds; the ultimate yield was 93%.

5-↓-Hydroxy-6-↓-chloromercuri-1,4-↑↑-methylenecyclohexane-2-↓-3-↑-dicarboxylic Acid, μ = 4.07 (XII)

(*a*) *By Isomerization of* XI (μ = *3.88 D*)

A solution of 41.7 g (0.10 mole) of 5-↓-hydroxy-6-↓-chloromercuri-1,4-↑↑-methylene-2,3-↓↓-dicarboxylic acid (μ = 3.88) in 400 ml (1.0 mole) of 10% aqueous sodium hydroxide was refluxed for 2 hours, then cooled slowly, finally chilled and acidified by acetic acid to pH 5. The precipitate, 12.65 g of impure diastereomer, μ = 3.88, melted at about 200°. The filtrate was made basic to pH 7.5, then was vacuum-evaporated to a 100-ml volume, and then was acidified cold to pH 2 with hydrochloric acid. The 15-g crop, m.p. about 190°, was dissolved in 50 ml of dimethylformamide, filtered, and treated with 80 ml of chloroform. After a precipitate (10 g, m.p. 206°) was filtered off, the filtrate was vacuum-evaporated. The residue was crystallized from 250 ml of boiling water to give 5 g (12%), m.p. 219–219.5°, strongly depressed by admixture with the diastereomer: μ, 3.88. Recrystallization from dimethylformamide–chloroform or from boiling water raised this melting point to 223–223.5° (sample inserted at 215°). Calc. for $C_9H_{11}O_5HgCl$: C, 24.8; H, 2.54. Found: C, 25.0; H, 2.75. The X-ray diffraction pattern was found to be [10] 12.10; [9] 5.12; [8] 3.56; [7] 3.07; [6] 4.67; [5] 6.23; [4] 6.65, 3.97; [3] 10.9, 5.94. The substance largely survived treatment with concentrated hydrochloric acid for 5 minutes but during 50 minutes it was converted to 1,4-↑↑-methylene-Δ^5-cyclohexene-2,3-↑↓-dicarboxylic acid (XIII), m.p. 184–185°, not depressed by mixture melting point with an authentic sample.

When the mercurial, μ = 4.07, was dissolved in cold alkali and potentiometrically titrated with standard hydrochloric acid it showed by three inflections (corresponding with 3 equivalents) that the substance was not a lactone. Treatment with acetic anhydride failed to convert this hydroxydicarboxylic acid to a γ-lactone.

(*b*) *By Oxymercuration of* XIII

A solution of 76.7 g (0.38 mole) of 1,4-↑↑-methylene-Δ^5-cyclohexene-2-↓-3-↑-dicarboxylic acid (XIII) in 3 liters of boiling water was treated with 103 g (0.38 mole) of mercuric chloride. The precipitating system was cooled to 25°, and then 300 ml (0.75 mole) of 10% aqueous sodium hydroxide was added (pH 5). After 8 hours the system was acidified to pH 2. The precipitate was filtered off, washed with methanol and ether, and then vacuum-dried, 145 g, m.p. 211–212°. This crude product was extracted with 1300 ml of boiling water leaving 132 g, m.p. 222–223°. A hot solution in dioxane (10 ml per g) precipitated about 70%, m.p. 217°. The remaining 30% was obtained from the filtrate by addition of an equal volume of diethyl ether and was nearly pure XII, m.p. 218–219°. The process should be repeated with the 70%, m.p. 217°, which yields less pure XII, m.p. 213–214°. All of the crops of XII (estimated total yield, 25%) may be purified by crystallization from boiling water (10 ml per g), m.p. 220–221°.

The aqueous filtrates and the initial precipitates from dioxane crystallizations are rich in XIV. After the latter had been removed as is described below the final aqueous filtrates yielded about 20 g of unchanged norbornenedicarboxylic acid, XIII.

5-↓-Hydroxy-6-↓-hydroxymercuri-1,4-↑↑-methylenecyclohexane-2-↓-3-↑-dicarboxylic Acid

A solution of 2.15 g (0.005 mole) of 5-↓-hydroxy-6-↓-chloromercuri-1,4-↑↑-methylenecyclohexane-2-↓-3-↑-dicarboxylic acid (XII) in 4 ml (0.01 mole) of 10% aqueous sodium hydroxide was shaken with 0.8 g (0.055 mole) of silver oxide for 2 hours, then filtered by suction to remove a mixture of silver oxide and chloride from which 0.70 g (98%) of the chloride was isolated by washing the mixture with nitric acid.

The filtrate from the mixture was acidified to pH 5.6 with acetic acid; the precipitate which appeared momentarily redissolved. When no precipitate appeared after 12 hours the system was further acidified to pH 5 with 10% aqueous acetic acid. The precipitate was filtered off and dissolved in 30 ml of 1% aqueous sodium hydroxide. The solution was clarified by means of Norite, then was filtered, and the filtrate was acidified with acetic acid. After 36 hours at 4° the precipitate was filtered off, 0.70 g (34%), m.p. 198°. Resolution in alkali with Norite treatment gave a solution from which no precipitate appeared upon saturation with carbon dioxide gas. Acidification by acetic acid to pH 5.2 gave a gelatinous precipitate (0.55 g), which was dissolved in alkali, treated with Norite, filtered, and acidified by use of acetic acid, m.p. 200.5–201°. Calc. for $C_9H_{12}O_6Hg$: C, 25.9; H, 2.90. Found: C, 25.8; H, 3.13.

When this substance was dissolved in dilute alkali, and then dilute hydrochloric acid was added, the melting point (221°) of the precipitate was not depressed by admixture with 5-↓-hydroxy-6-↓-chloromercuri-1,4-↑↑-methylenecyclohexane-2-↓-3-↑-dicarboxylic acid (XII).

5-↓-Hydroxy-1,4-↑↑-methylenecyclohexane-2-↓-3-↑-dicarboxylic Acid

A solution of 1.08 g (0.0025 mole) of 5-↓-hydroxy-6-↓-chloromercuri-1,4-↑↑-methylenecyclohexane-2-↓-3-↑-dicarboxylic acid (XII) in 4 ml (0.005 mole) of 5% aqueous sodium hydroxide was chilled to 4°, and 6.5 g (0.01 atom Na) of sodium amalgam was added at once. Next day the system was filtered and the chilled filtrate was acidified with concentrated hydrochloric acid. The crystalline precipitate (0.24 g) melted at 210–211°, decomp. The chilled filtrate after 5 days yielded 0.12 g, m.p. 209–210° (total 72%). The whole was crystallized from 1.5 ml of hot water and also from hot ethyl acetate, m.p. 210–211°, decomp. A mixture melting point with 5-↑-hydroxy-1,4-↑↑-methylenecyclohexane-2-↓-3-↑-dicarboxylic acid was lowered to 192°. Calc. for $C_9H_{12}O_5$: C, 54.1; H, 6.04. Found: C, 54.1; H, 6.14. The X-ray diffraction pattern is [10] 5.30; [9] 4.38, 4.79; [8] 3.38; [6] 5.68, 3.65; [5] 4.23; [4] 5.98; [3] 3.79, 2.70, 3.22; [2] 2.79, 2.97; [1] 2.16, 2.00, 2.50.

5-↓-Hydroxy-6-↑-chloromercuri-1,4-↑↑-cyclohexane-2-↑-3-↓-dicarboxylic Acid, γ-Lactone, $\mu = 6.40$ (XIV)

(*a*) *By Oxymercuration*

After the product obtained by treatment of 0.38 mole of 1,4-↑↑-methylene-Δ^5-cyclohexene-2-↓-3-↑-dicarboxylic acid was extracted to remove XII there remained impure crops (m.p. 208–213°) from dioxane crystallizations, and also filtrates from aqueous extractions and crystallizations. The latter were vacuum-evaporated and the whole was dissolved in hot water (10 ml per g), cooled, and filtered. Evaporation of the filtrates to 1/2–1/3 volume gave precipitates of XIV melting at 228–236°. These crops represent a

total isolable yield of about 40% of theoretical. The final purification was effected by crystallization from hot dioxane (23 ml per g), m.p. 237–238°. Calc. for $C_9H_9ClHgO_4$: C, 25.7; H, 2.18. Found: C, 25.3; H, 2.43. The X-ray diffraction pattern was [10] 13.5; [9] 8.97; [8] 7.29; [7] 10.45; [4] 3.66; [3] 4.27; [2] 6.19, 5.04; [1] 3.01. Treatment for 1 hour with twice its weight of concentrated hydrochloric acid converted the mercurial into 1,4-↑↑-methylene-Δ^5-cyclohexene-2-↓-3-↑-dicarboxylic acid, m.p. 186–187°, authenticated by mixture melting point.

When a solution of 150 mg of this mercurial (μ = 6.40 D) and 150 mg of 5-↓-hydroxy-6-↓-chloromercuri-1,4-↑↑-methylenecyclohexane-2-↓-3-↑-dicarboxylic acid (μ = 4.07 D) in 80 ml of dioxane was treated with 0.5 ml of concentrated hydrochloric acid for 3 hours the vacuum-evaporated system could be extracted with chloroform to yield only one mercurial, which, crystallized from water, melted at 230°, 60 mg, with powder diagram identical with that shown above for the compound, μ = 6.40 D. The chloroform-insoluble portion yielded 1,4-↑↑-methylene-Δ^5-cyclohexene-2-↓-3-↑-dicarboxylic acid, m.p. 186–187°, with X-ray powder diagram [10] 4.99; [5] 4.34; [4] 3.92; [2] 4.61, 4.51, 3.44, 3.19; [1] 6.43, 5.62, 3.01, 2.95, 2.68. This pattern is in contrast to that determined for 1,4-↑↑-methylene-Δ^5-cyclohexene-2,3-↓↓-dicarboxylic acid, m.p. 179–180°, which is [10] 6.10; [9] 4.44; [8] 4.23; [5] 4.95; [3] 3.86, 3.25; [2] 2.79, 2.73; [1] 5.47, 5.18, 5.06, 3.49, 2.39. The reader is cautioned about the subtle difference between this latter pattern and that of the product of platinum-catalyzed reduction, 1,4-↑↑-methylenecyclohexane-2,3-↓↓-dicarboxylic acid, m.p. 161–161.5°: [10] 6.25; [9] 4.45; [8] 4.32; [5] 5.05; [3] 3.91, 3.35, 3.27, 2.79, 2.48; [2] 5.23; [1] 5.62, 5.45, 3.82, 2.93, 2.72.

A solution of 0.86 g (0.002 mole) of 5-↓-hydroxy-6-↑-chloromercuri-1,4-↑↑-methylenecyclohexane-2-↑-3-↓-dicarboxylic acid, γ-lactone, in 4 ml (0.005 mole) of 5% aqueous sodium hydroxide was chilled and treated at once with 5.2 g (0.008 atom Na) of 3.5% sodium amalgam. After 7 hours the system was filtered and the chilled filtrate was acidified strongly with concentrated hydrochloric acid. The crystals, 0.25 g, m.p. 127–128° (70%), were recrystallized from benzene (50 ml per g), m.p. 132–133.5°. A mixture melting point with 5-↓-hydroxy-1,4-↑↑-methylenecyclohexane-2-↑-3-↓-dicarboxylic acid, γ-lactone, was not depressed.

(*b*) *By Isomerization*

A mixture of 1.82 g (0.0032 mole) of 5-↓-hydroxy-6-↑-chloromercuri-1,4-↑↑-methylenecyclohexane-2,3-↓↓-dicarboxylic acid, γ-lactone (X, μ = 7.18), and 0.82 g (0.0032 mole) of mercurous acetate in 25 ml of methanol was refluxed for 8 hours. Then it was diluted with water and made slightly alkaline. Darco was added and the dirty yellow precipitate was filtered off. The filtrate was acidified by addition of acetic acid to yield 1.00 g of chloride-free precipitate of indistinct melting point.

This precipitate was refluxed 3 hours in 20 ml of 4% aqueous sodium hydroxide, then chilled and acidified to pH 5.0 by addition of acetic acid. After 12 hours 0.48 g of infusible precipitate was filtered off. The filtrate upon acidification to pH 2 with dilute hydrochloric acid yielded 0.22 g, m.p. 233–235°, not depressed by admixture with the mercurial, μ = 6.40, prepared by oxymercuration, but was depressed by the mercurials X (μ = 7.18) and XII (μ = 4.07).

The infusible precipitate, 0.48 g, was dissolved in 10% aqueous sodium chloride and then was acidified with 12% hydrochloric acid. The precipitate, m.p. 211–213°, was crystallized from water, m.p. 223–224°, not depressed by admixture with the reagent mercurial, X.

5-↓-Hydroxy-6-↑-chloromercuri-1,4-↑↑-methylenecyclohexane-2,3-↓↓-dicarboxylic Acid, γ-Lactone, μ = 7.18 D (X)

To a solution of 1.13 g (0.005 mole) of stannous chloride dihydrate in 50 ml (0.02 mole) of 1.6% aqueous sodium hydroxide was added 4.00 g (0.01 mole) of 5-↓-hydroxy-anhydro-[6-↓-hydroxymercuri-2-↓-carboxy]-1,4-↑↑-methylenecyclohexane-3-↓-carboxylic acid (11) and then 2.7 cc (0.0068 mole) more of aqueous 10% sodium hydroxide; final pH was 8. After 1 hour the black precipitate was filtered off. The cold filtrate was strongly and quickly acidified with 12% hydrochloric acid in order to redissolve the precipitated tin salts; then a granular precipitate appeared. After 12 hours the precipitate was filtered off and washed with water, 1.95 g (47%), m.p. 204–205°. Crystallization from methanol (0.6 g per ml, Darco) raised this melting point to 225.5–226°. Mixture melting points with the mercurials of moments of 3.88, 4.07, and 6.40 D all were depressed. X-Ray diffraction pattern is [10] 6.70; [7] 12.10; [5] 6.15, 5.02, 4.88, 4.00, 3.62, 3.14; [4] 3.32, 2.74, 5.32, 4.38; [1] 4.58, 4.22, 3.07. Calc. for $C_9H_9ClHgO_4$: C, 25.7; H, 2.17. Found: C, 26.2; H, 2.31.

When 0.10 g of this product and of the diastereomeric mercurial, μ = 3.88 D, were mixed and treated with 0.5 ml of concentrated hydrochloric acid for 5 minutes the diluate with an equal volume of water yielded 6 mg with X-ray diffraction pattern corresponding with the product, μ = 7.18 D. When the latter was treated alone with 1.4 times its weight of concentrated hydrochloric acid for 45 minutes at least 30% of it survived, m.p. 216–217°, not depressed by admixture with the pure reagent, μ = 7.18 D. However, a reaction period of 12 hours yielded only 5-↓-hydroxy-1,4-↑↑-methylenecyclohexane-2,3-↓↓-dicarboxylic acid, γ-lactone, m.p. 202°, not depressed by admixture with the authentic lactone (35). The lactone was characterized further by methylation as described below.

5-↓-Hydroxy-2-↓-carbomethoxy-1,4-↑↑-methylenecyclohexane-3-↓-carboxylic Acid, γ-Lactone

A solution of 7.28 g (0.04 mole) of 5-↓-hydroxy-1,4-↑↑-methylenecyclohexane-2,3-↓↓-dicarboxylic acid, γ-lactone, m.p. 201–202°, in 32 ml (0.08 mole) of 10% aqueous sodium hydroxide was heated to boiling for several minutes, then cooled to 25°, and 6.72 g (0.08 mole) of sodium bicarbonate was added in 50 ml of water. Then 15.2 ml (0.16 mole) of dimethyl sulphate was added and the system was stirred for 2 days. The whole was then exhaustively extracted with chloroform. The evaporated extracts were crystallized from water, 4.79 g, 61%, m.p. 76–77°. This product was crystallized from benzene – commercial hexane (1:1, 40 ml per g), m.p. 81–82°. X-Ray diagram was [10] 5.38; [8] 4.73; [6] 6.53; [5] 3.99, 3.50, 3.39; [3] 3.81, 2.85; [2] 5.94, 4.38, 3.27; [1] 7.59, 4.94, 2.27. Calc. for $C_{10}H_{12}O_4$: C, 61.3; H, 6.17. Found: C, 61.3; H, 6.23.

5-↓-Hydroxy-2-↑-carbomethoxy-1,4-↑↑-methylenecyclohexane-3-↓-carboxylic Acid, γ-Lactone

When 1.96 g (0.01 mole) of 5-↓-hydroxy-2-↓-carbomethoxy-1,4-↑↑-methylenecyclohexane-3-↓-carboxylic acid, γ-lactone, m.p. 81–82°, was treated for 45 minutes with a solution of 0.23 g (0.01 atom) of sodium in 15 ml of methanol and then with 0.95 ml (0.01 mole) of dimethyl sulphate a rise in temperature was observed at the last step. After 1 hour the solvent was removed under vacuum and replaced with water. The product (1.46 g, 70%, m.p. 67–68°) was crystallized from boiling ethyl ether (1.2 ml per g), m.p. 68.3–68.8°. X-Ray diagram: [10] 5.15; [9] 4.59; [5] 5.64; [3] 6.60, 4.23; [2] 3.83, 3.46, 2.87; [1] 3.68, 2.58, 2.11. This substance was recovered unchanged after 6 hours with 1 equivalent of 10% aqueous mercuric acetate. When the substance was saponified during 1 hour with 10% aqueous alkali at 80° or was hydrolyzed by concentrated hydro-

chloric acid during 1 minute it yielded 5-↓-hydroxy-1,4-↑↑-methylenecyclohexane-2-↑-3-↓-dicarboxylic acid, γ-lactone, m.p. 132.8–133°, authentic according to mixture melting point and elemental analysis. Calc. for $C_{10}H_{12}O_4$: C, 61.3; H, 6.17. Found: C, 61.8; H, 6.32.

1,4-↑↑-Methylene-Δ⁵-cyclohexene-2,3-↑↓-dicarboxylic Acid (XIII)

When prepared by sodium methoxide saponification of dimethyl 1,4-↑↑-methylene-Δ⁵-cyclohexene-2,3-↓↓-dicarboxylate (35) the compound melted at 186.5° after crystallization from hot acetonitrile (25 ml per g). The powder diagram is reported above.

Dimethyl 5-↑-Acetoxy-6-↓-chloromercuri-1,4-↑↑-methylenecyclohexane-2,3-↓↓-dicarboxylate (XXIII, Z = CH_3CO, X = Cl)

(*a*) *In 2,5-Dioxahexane*

To a solution of dimethyl 1,4-↑↑-methylene-Δ⁵-cyclohexene-2,3-↓↓-dicarboxylate (m.p. 37°, 1.05 g, 0.0047 mole) in 10 ml of anhydrous 2,5-dioxahexane was added 1.45 g (0.0046 mole) of mercuric acetate. After 74 hours of agitation the system (in which all of the solid had dissolved) was poured into 40 ml of 2.5% aqueous sodium chloride. The oil soon crystallized, 1.925 g (83%), m.p. 153–158°. Four crystallizations from methanol raised the melting point to 177°. Diffraction pattern was [10] 5.64; [9] 6.41; [8] 11.47, 6.96; [7] 4.80, 3.88; [6] 3.23; [4] 4.50, 3.66; [3] 4.17, 3.48. Calc. for $C_{13}H_{17}ClHgO_6$: C, 30.9; H, 3.38; OCH_3, 12.3. Found: C, 30.6; H, 3.54; OCH_3, 12.1.

(*b*) *In Methanol*

To 2.10 g (0.01 mole) of the dimethyl ester in 35 ml of anhydrous methanol was added 3.18 g (0.01 mole) of mercuric acetate. The salt dissolved during 25 minutes. After 8 hours the system was filtered into 100 ml of 5% aqueous sodium chloride. The precipitate (4.57 g, 95%, m.p. 163–165°) was crystallized from absolute methanol (25 ml per g), m.p. 171–172°.

(*c*) *In Acetic Acid*

A solution of 10.5 g (0.047 mole) of the ester used in procedure (*a*) and 14.5 g (0.046 mole) of mercuric acetate in 50 ml of glacial acetic acid was let stand for 12 hours, then was poured into 350 ml of 3% aqueous sodium chloride. The precipitate was filtered off after 1 hour, washed with water and with methanol, and vacuum-dried, 22.1 g (93%), m.p. 173–174°. Crystallization from methanol (55 ml per g) raised this melting point to 177–177.2° (11.4 g). Subsequent crops, m.p. 175–168°, obtained by chilling and by concentration of the mother liquor finally left a filtrate which was vacuum-evaporated. The residue was twice purified by solution in warm dimethylformamide (12 ml per g), filtration of the slight precipitate appearing at 25°, and then dilution with an equal volume of chloroform. The product (0.13 g, 0.5%), m.p. 229–229.5°, was found to be 5-↓-hydroxy-6-↓-chloromercuri-2-↓-carbomethoxy-1,4-↑↑-methylenecyclohexane-3-↓-carboxylic acid, γ-lactone (XXII, X = Cl) (11). Identification was made by mixture melting point after it was found that the substance prepared from the ester and mercuric acetate in water also melted at 229° (rather than 223.5°) after sufficient purification. The two products gave the same X-ray powder pattern.

When 3 g of the dimethyl 5-↑-acetoxy-6-↓-chloromercuri-1,4-↑↑-methylenecyclohexane-2-↓-3-↑-dicarboxylate was reduced by 2 g of lithium aluminum hydride in tetrahydrofuran (slow addition followed by reflux) with hydrolysis by aqueous ammonium chloride, the product, m.p. 78-84°, weight 0.85 g, upon crystallization from commercial pentane

melted at 81.5–83°. It reacts rapidly with alkaline permanganate to yield a product which may be 2,3-dimethylol-1,4-↑↑-methylene-Δ^5-cyclohexene.

5-↑-Hydroxy-6-↓-chloromercuri-1,4-↑↑-methylenecyclohexane-2-↓-3-↑-dicarboxylic Acid (XXIV)

A solution of 5.15 g (0.01 mole) of dimethyl 5-↑-acetoxy-6-↓-chloromercuri-1,4-↑↑-methylenecyclohexane-2,3-↓↓-dicarboxylate in 36 ml (0.09 mole) of 10% aqueous sodium hydroxide was maintained at room temperature for 15 hours, then chilled and acidified cautiously to pH 2 with concentrated hydrochloric acid. The precipitation which commenced after 15 minutes was complete after 1 day at 4°. Filtration gave 2.59 g (60%), m.p. 183–184° (inserted at 160°). Quick crystallization from boiling water (10 ml per g) raised this melting point to 184–184.5°. The X-ray diffraction pattern was [10] 4.21, 5.05; [9] 5.79; [8] 5.60; [7] 3.44; [6] 3.26, 3.14; [5] 3.03; [3] 2.39; [2] 2.74; [1] 2.66, 3.91. The infrared band spectrum of polyethylene wax pellets (6000 p.s.i. at 23°) containing 5% is reported in wave numbers [cm^{-1}] at specified per cent transmissions: [316] 46; [352] 82; [388] 85; [410–17] 88; [428] 76; [451] 83; [553] 73; [648] 50; [678] 68; [794] 68; [884] 53. The density of the solid at 23° was 2.420 and the extrapolated dielectric constant of pellets was 3.917, so P_{e+a} is 88.5 cc. Calc. for $C_9H_{11}ClHgO_5$: C, 24.9; H, 2.56. Found: C, 25.0; H, 2.70.

When this substance was dissolved and boiled in water (7–8 ml per g) for 15 minutes the crystals which separated upon cooling melted first at 216–217° and then after an identical crystallization at 221–222°. The X-ray diffraction pattern was [10] 9.65; [9] 5.80; [8] 3.64; [7] 7.22; [6] 4.21, 4.25; [5] 4.56, 4.83, 5.26; [4] 3.22, 3.07; [3] 3.35, 3.50; [2] 2.94; [1] 2.82. The infrared band spectrum (5% in polyethylene wax compressed at 6000 p.s.i.) was recorded in [cm^{-1}] at indicated per cent transmissions: [316.8] 42; [351] 75; [390] 76; [414] 76; [429] 66; [453] 71; [550] 58; [649] 42; [675] 54; [696–702] 55; [791] 42; [841] 40; [881] 35. The density of the solid substance at 23° was 2.453 and the dielectric constants of pellets of various thicknesses were extrapolated to zero thickness for $\epsilon = 4.019$, whence P_{e+a} is 88.9 cc. Calc. for $C_9H_{11}ClHgO_5$: C, 24.9; H, 2.56. Found: C, 24.7; H, 2.53.

The melting point was not depressed when the substance was quickly crystallized from water or other solvents, but when it was dissolved in alkali and then reprecipitated by addition of hydrochloric acid the modification, m.p. 184–185°, reappeared. The latter could again be converted to the 221–222° variety by 15-minute reflux in boiling water. The high melting variety decomposed completely when heated under vacuum at its melting point and did not yield any of compound XIV. The filtrate from the original acidified reaction system was found to yield at least 0.59 g of 1,4-↑↑-methylene-Δ^5-cyclohexene-2,3-↓↑-dicarboxylic acid, m.p. 187°. Treatment of the mercurial with concentrated hydrochloric acid also gave this product, authenticated by mixture melting point.

It was observed that the low melting 5-↑-hydroxy-6-↓-chloromercuri-1,4-↑↑-methylenecyclohexane-2-↓-3-↑-dicarboxylic acid at its melting point tended oftentimes to resolidify after melting. This property was utilized by heating 0.2 g, m.p. 184–185°, in a test tube under continuous water aspirator vacuum by immersion into a paraffin bath heated from 185° to 193° during 15 minutes. After cooling to 25° the residue was extracted with 10 ml of hot acetone. This extract was treated with commercial hexane to incipient turbidity. After several hours the system was filtered to remove a slight precipitate. Then the filtrate was vacuum-evaporated to leave a syrup which solidified when moistened with methanol. The solid product, 0.08 g (24%), melted at 232–232.5°, and was found

by mixture melting point to be identical with 5-↓-hydroxy-6-↑-chloromercuri-1,4-↑↑-methylenecyclohexane-2-↑-3-↓-dicarboxylic acid, γ-lactone (m.p. 234°). The X-ray diffraction pattern also was identical with that of XIV.

5-↑-Hydroxy-1,4-↑↑-methylenecyclohexane-2-↓-3-↑-dicarboxylic Acid

A solution comprised of 129.6 g (0.3 mole) of 5-↑-hydroxy-6-↓-chloromercuri-1,4-↑↑-methylenecyclohexane-2-↓-3-↑-dicarboxylic acid in 480 ml (0.6 mole) of 5% aqueous sodium hydroxide was prepared during 2 hours of stirring. Then 442 g (0.66 atom Na) of 3.5% sodium amalgam was added with stirring during 2 hours, the temperature being maintained at 33°. Five hours later the system was filtered, chilled, strongly acidified by addition of 75 ml of concentrated hydrochloric acid, and continuously extracted with diethyl ether. The first 14-hour extract contained 7.9 g of unchanged mercurial as ether-insoluble material. Subsequently the extraction was continued for 40 hours longer.

The total extract (except for unchanged mercurial) was evaporated, dissolved in 200 ml of ethyl acetate, and then placed on a chromatographic column, 70 mm O.D. by 150 cm long of 100–170-mesh silica gel which had been deactivated by washing with U.S.P. chloroform. The column was first eluted with 4 liters of chloroform and the eluate was discarded. Likewise the first 2 liters of eluate were discarded after 2 liters of 1:1 chloroform – ethyl acetate (purified) and then pure ethyl acetate was used for elution. The next 1.5 liters yielded about 10 g of 1,4-↑↑-methylene-Δ^5-cyclohexene-2-↓-3-↑-dicarboxylic acid, m.p. 182–183°. The subsequent eluant (5 liters) yielded a semisolid upon evaporation which was crystallized from hot ethyl acetate to yield 55 g, m.p. 155–160° (90%). Recrystallization from ethyl acetate raised this melting point to 184.5°. The crystallization is accomplished by solution in 10–20 ml of solvent per gram after which 40% of the solvent is distilled off. The rate of crystal growth usually requires 4 to 5 days. Calc. for $C_9H_{12}O_5$: C, 54.1; H, 6.08. Found: C, 53.9; H, 6.04. The X-ray diffraction pattern was [10] 4.21, 5.05; [9] 5.79; [8] 5.60; [7] 3.44; [6] 3.26, 3.14; [5] 3.03; 3] 2.39; [2] 2.74; [1] 2.66, 3.91.

5-↓-Hydroxy-6-↓-chloromercuri-2-↓-carbomethoxy-1,4-↑↑-methylenecyclohexane-3-↓-carboxylic Acid, γ-Lactone (XXII, X = Cl)

A solution of 7.95 g (0.025 mole) of mercuric acetate in 80 ml of water was shaken with 5.25 g (0.025 mole) of molten dimethyl 1,4-↑↑-methylene-Δ^5-cyclohexene-2,3-↓↓-dicarboxylate (m.p. 37.5–38°) until the oil dissolved (8 minutes). Thirty minutes later the system was shaken vigorously while a solution of 1.5 g of sodium chloride in 5 ml of water was added slowly. The crude precipitate, methanol-washed and vacuum-dried, weighed 10.2 g, m.p. 201–203° (95%). This product was dissolved in 35 ml of dimethylformamide at 100°. The precipitate formed upon cooling weighed 6.45 g, m.p. 229–229.5° (60%). A methoxyl analysis showed 7.31% OCH_3, calc. 7.19%. The strongest lines of the X-ray diffraction pattern are [10] 9.30; [9] 4.61; [8] 3.61; [7] 2.92; [6] 5.81; [5] 6.55, 2.43; [4] 2.04. Recrystallization from dimethylformamide raised the melting point to 230.5–231°.

When this ester lactone (0.5 g) was dissolved in 1 ml of concentrated hydrochloric acid and the solution, after 12 hours, was diluted with water and let stand 1 week, crystals were obtained. The product, 0.115 g, m.p. 195–196°, was crystallized from hot water, m.p. 201°. A mixture melting point with 5-↓-hydroxy-1,4-↑↑-methylenecyclohexane-2,3-↓↓-dicarboxylic acid, γ-lactone, was not lowered.

Saponification of the pure ester lactone was effected by maintaining a solution of 2.57 g (0.005 mole) in 18 ml (0.045 mole) of 10% aqueous sodium hydroxide for about 12 hours after which the system was boiled for ½ hour. Acidification with 12% hydrochloric

acid gave 1.96 g, m.p. 181°. Extraction with 40 ml of boiling water left 0.70 g, m.p. 219–220°, which was not lowered by admixture with XI. The cooled filtrate gave 0.68 g, m.p. 196–197°, from which successive crops of XI could be obtained. The final crop, 0.33 g, melted at 209–210° and was impure 5-↓-hydroxy-6-↓-chloromercuri-1,4-↑↑-methylenecyclohexane-2-↓-3-↑-dicarboxylic acid (XII) of X-ray diffraction pattern [10] 5.14; [8] 12.02; [7] 3.55, 3.94; [5] 3.07; [4] 4.30; [3] 4.47, 6.25; [2] 5.92, 6.73; [1] 10.84, 3.74.

A by-product was also found to be formed in the oxymercuration. When the dimethylformamide contained in the mother liquors from crystallization of the 10.2 g portion (above) was evaporated the residue upon quick crystallization from boiling water melted at 181°. After another quick crystallization it melted at 187–188° and resolidified to melt again at 214°. These properties identify it as 5-↑-hydroxy-6-↓-chloromercuri-1,4-methylenecyclohexane-2-↓-3-↑-dicarboxylic acid (XXIV). Further proof was obtained by heating 0.2 g under vacuum from 195 to 204° during 20 minutes. An acetone extract of the cooled residue, evaporated and treated with methanol, gave 0.05 g of 5-↓-hydroxy-6-↑-chloromercuri-1,4-methylenecyclohexane-2-↑-3-↓-dicarboxylic acid, γ-lactone (XIV), m.p. 232–233°, with partial X-ray diagram [10] 7.13; [9] 5.65; [7] 2.35; [6] 3.50; [5] 2.84; [4] 4.05.

Dimethyl 5-↑-Methoxy-6-↓-chloromercuri-1,4-↑↑-methylenecyclohexane-2,3-↓↓-dicarboxylate (XXIII, Z = Me, X = Cl)

To a solution of dimethyl 1,4-↑↑-methylene-Δ^5-cyclohexene-2,3-↓↓-dicarboxylate (1.05 g, 0.0047 mole) in anhydrous methanol containing 0.5 g (0.0035 mole) of boron fluoride etherate was added 1.58 g (0.005 mole) of mercuric acetate. After 4 minutes the salt dissolved, and after 10 minutes the whole was poured into 50 ml of 5% aqueous sodium chloride. After 2 days at 4° the precipitate was filtered, water-washed, and dried, 1.78 g, m.p. 97–121°. This mixture of acetoxy- and methoxy-mercurials was fractionally crystallized from ethyl acetate – isooctane solutions to give impure acetoxymercurial (X-ray diffraction pattern) and pure dimethyl chloromercurimethoxymethylenecyclohexanedicarboxylate, 0.5 g (10%), m.p. 130–131°. X-Ray diffraction pattern is [10] 6.96; [9] 3.97; [8] 5.34; [7] 3.42, 3.08; [6] 4.62; [5] 5.94, 4.27; [4] 2.91. A longer reaction time (36 hours) gave a lower weight yield (1.55 g) of higher (107–114°) melting point. Calc. for $C_{12}H_{17}ClHgO_5$: C, 30.2; H, 3.56; OCH_3, 19.5. Found: C, 30.4; H, 3.64; OCH_3, 19.1.

When XXIII was treated with concentrated hydrochloric acid, and after 1 hour, the system was evaporated to 20% of the original volume crystals of 5-↓-hydroxy-1,4-↑↑-methylenecyclohexane-2,3-↓↓-dicarboxylic acid, γ-lactone, appeared, m.p. 198°. Crystallization from water raised this melting point to 201–202° and a mixture melting point with an authentic sample was not lowered.

5-↑-Methoxy-1,4-↑↑-methylene-2,3-↑↑-[1′-↑-hydroxy-Δ^2-propene-1′,3′-ylene]-cyclohexane

A solution of 5-↑-methoxy-1,4-↑↑-methylene-2,3-↑↑-propenylenecyclohexane (prepared in 92% yield by use of sodamide rather than sodium (36)) in 200 ml of pure acetic anhydride was added dropwise to a stirred ice-cooled suspension of selenium dioxide (67.2 g, 0.6 mole) in 25 ml of water. Following then a comparable procedure (37), an acetate, b.p. 147° (12 mm), was obtained, n_D^{20} 1.4974, 87 g, 65%, % C, 71.0, % H, 8.40. Hydrolysis by the prescribed method gave an 83% yield of the methoxy alcohol, b.p. 148° (11 mm), n_D^{20} 1.5145. Calc. for $C_{11}H_{16}O_2$: C, 73.3; H, 8.88; Found: C, 73.8; H, 8.78.

5-↑-Methoxy-1,4-↑↑-methylene-2,3-↑↑-propenonylenecyclohexane

Following the recommended procedure (37) upon the methoxy alcohol described above an 83% yield was obtained, b.p. 147° (11 mm), n_D^{20} 1.5188, λ_{max} 225 mμ, E_{max} 8,650. Calc. for $C_{11}H_{14}O_2$: C, 74.1; H, 7.85. Found: C, 73.7; H, 7.70.

5-↑-Methoxy-1,4-↑↑-methylenecyclohexane-2,3-↑↑-dicarboxylic Acid

To a stirred solution of the unsaturated ketone (1.5 g) in 30 ml of acetone plus 1 ml of water was added 8 g of potassium permanganate during 10 minutes (37); the system boiled. After 2 hours of stirring 10 ml of water was added, followed by 20 ml of methanol. After 30 minutes the permanganate was reduced so the manganese dioxide was filtered off and washed with acetone and water. The residue from the vacuum-evaporated filtrate was dissolved in 10 ml of water and the solution acidified to pH 4 was saturated with sodium chloride and thoroughly extracted by ethyl ether. The extracts, evaporated, left 1.1 g of sticky solid which was crystallized from benzene–methanol and from water to give 0.68 g, m.p. 149–152°. Crystallization from methanol – ethyl acetate gave 0.37 g, m.p. 166–167°. Calc. for $C_{10}H_{14}O_5$: C, 56.0; H, 6.58. Found: C, 56.4; H, 6.73. X-Ray diffraction pattern is [10] 4.99; [9] 5.73; [8] 3.91; [7] 4.26; [6] 5.45.

Stability of Mercurials Toward Concentrated Hydrochloric Acid

After 1 year a suspension of 0.2 g of butylmercuric chloride in 2 ml of concentrated hydrochloric acid at room temperature was filtered to recover 0.19 g of the mercurial. The filtrate was evaporated to a volume of 1 ml and then was made basic with aqueous sodium hydroxide. No mercuric oxide was precipitated. The result was unaltered by inclusion of 0.01 g of mercurous chloride into the system.

A suspension of 0.1 g of cyclopentylmercuric chloride in 2 ml of concentrated hydrochloric acid and 1 ml of dioxane was refluxed for 1 day. The mercurial was all recovered unchanged, m.p. 112°. The inclusion of 0.01 g of mercuric chloride did not alter this result.

A mixture of 0.200 g each of β-2-chloromercuricineole and of phenylmercuric chloride in 2 ml of methanol was treated with 2 ml of concentrated hydrochloric acid. The system, which became warm, was cooled to room temperature and was stirred for 30 minutes. After dilution with water the solid phase was filtered off, 0.175 g, m.p. 255–256°, which was proved by mixture melting point to be phenylmercuric chloride. Addition of alkali to the filtrate gave 0.258 mmole of mercuric oxide.

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PRESSURE EFFECT AND MECHANISM IN ACID CATALYSIS

V. THE HYDROLYSIS OF ACETIC ANHYDRIDE[1]

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ABSTRACT

The spontaneous and the acid-catalyzed hydrolyses of acetic anhydride have been measured as a function of temperature over the range 0 to 40° C, as a function of pressure over the range 0 to 3 kb at 0° C, and as a function of solvent over the range 0 to 70.3% w/w acetone–water at 0° C. The results are discussed with reference to the mechanisms of the hydrolyses. The volume and entropy of activation of the acid-catalyzed hydrolysis are $-17.1 \pm \sim 1.3$ cm^3 mole^{-1} and ~ -20 cal deg^{-1} mole^{-1}, showing that the mechanism

$$Ac_2\overset{+}{O}H \rightarrow AcOH + Ac^+,$$

suggested because the rate was proportional to Hammett's h_0, is not correct. It follows that the Zucker–Hammett hypothesis is invalid for this reaction, as we have shown previously for other reactions, and hence that it does not provide a valid method of distinguishing between the A-1 and A-2 mechanisms.

1. INTRODUCTION

The acid-catalyzed hydrolysis of acetic anhydride has been studied by Kilpatrick (1) and by Gold and Hilton (2, 3). It is usually accepted that the first step in the hydrolysis is the equilibrium transfer of a proton to the anhydride. The second step is most likely either a unimolecular decomposition of the conjugate acid (A-1 mechanism) or a bimolecular addition of or substitution by a water molecule (A-2 mechanism). Gold and Hilton (2) measured the rate constants in concentrated acids and found that the first-order constants were much more nearly proportional to Hammett's acidity function h_0 than to hydrogen-ion concentration. They deduced from this that the mechanism is most likely A-1. However, we have shown in previous papers (4, 5) that some reactions that follow h_0 rather than hydrogen-ion concentration are actually A-2, and so the conclusion of Gold and Hilton is doubtful. We have also shown (4, 5, 6, 7) that the pressure coefficient of an acid-catalyzed reaction can help to elucidate mechanism, and in this paper we report a study of the effect of pressure on the acid-catalyzed hydrolysis of acetic anhydride. There are many possible mechanisms. First, there are two possible locations of the proton in the conjugate acid, the carbonyl oxygen and the ether oxygen. Both forms can react by an A-1 decomposition, an A-2 substitution by water, or an A-2 addition of water, which may be either slow, or fast and followed by a slow step. Consequently, unique conclusions are not to be expected. In order to accumulate useful information the effects of temperature and solvent composition have also been studied.

In order to follow the acid-catalyzed reaction it is necessary to study the spontaneous reaction, and similar measurements have been made for this reaction.

2. EXPERIMENTAL METHODS

Reagent-grade acetic anhydride and acetone, and technical-grade aniline distilled in the presence of zinc and solid sodium hydroxide, were used. The acetone–water solvent mixtures were made up by volume at 25° C.

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The high-pressure technique was essentially that described in Part II (7). The apparatus has been somewhat improved by using heavier-walled capillary tube to connect the syringe to the valve, so reducing the number of breakages of the tube, and by measuring the pressures at 1000 b and higher by means of a 3-kb Heise Bourdon gauge of accuracy about 0.1%. Runs at 1 b were done in stoppered flasks.

Initial concentrations of acetic anhydride were 0.1–0.2 *M*. For reactions that were acid-catalyzed the acetic anhydride was dissolved in standard acid. Both reactant and solvent were heated or cooled to the temperature of the experiment before mixing. Analysis was done by pipetting 1 to 5 ml of solution (chosen to give a final titer of about 50 ml of barium hydroxide) into 0.3 *M* aqueous aniline. Acetic anhydride reacts quantitatively and rapidly with aniline to give acetanilide and acetic acid; the acetic acid was titrated, together with the acid catalyst and the acetic acid already produced by hydrolysis, with standard barium hydroxide. The difference between the titer and that of a fully hydrolyzed sample is proportional to the anhydride concentration. The half-lives were, at the higher temperatures, rather short, and the pipettes used for taking samples were cooled or heated to the temperature of the experiment; the sample was blown in about 2 seconds from the pipette to the aniline solution, and the time at which this occurred was the time corresponding to the sample. The smallest half-life for the high-pressure experiments was about 1½ hours, so the sampling introduced only a very small error.

The reactions were kinetically of first order up to 75% of complete reaction. The first-order rate constant k is the sum of spontaneous and acid-catalyzed terms, thus

$$k = k_0 + k_a c_{H^+},$$

where k_0 is the first-order constant for the spontaneous reaction, k_a the second-order constant for the acid-catalyzed reaction, and c_{H^+} is the concentration of hydrogen ion. The spontaneous and acid-catalyzed rate constants were calculated from measurements in pure solvent and in acidified solvent respectively. It was calculated from the final values of k_0 and k_a and the dissociation constants of acetic acid in the solvents used, assuming these to be the same as in water–dioxane mixtures (8) of the same dielectric constant as the water–acetone mixtures, that catalysis by hydrogen ions derived from the acetic acid produced in the hydrolysis is negligible. This is verified by the linear first-order plots.

The 0° C bath was maintained by ice; in order to reduce corrosion of the high-pressure equipment small amounts of sodium dihydrogen phosphate were added to the bath, so its temperature was not exactly 0° C. Small corrections ($< 2\%$) were made to convert the rate constants to 0° exactly using the Arrhenius equation.

The reproducibility of the rate constants was about 1½%, and the accuracy is probably about 2%.

3. RESULTS

Spontaneous Hydrolysis

The rate constants for the spontaneous hydrolysis are given as a function of temperature, pressure, and composition, in Table I. The only direct comparison with other measurements that can be made is for pure water at 0° C and 1 atm. Under these conditions Kilpatrick (1) found $k_0 = 432\times10^{-6}$ sec^{-1}, and Gold (9) found 460×10^{-6} sec^{-1}, in satisfactory agreement with the mean of our values, 468×10^{-6} sec^{-1}. Other results of Gold cannot be compared directly with ours because they were not measured at common

TABLE I

Rate constants for the spontaneous hydrolysis of acetic anhydride

Temp., °C	% w/w of acetone in solvent	p/b	$10^6 k_0$/sec^{-1}
0	0	1	464 451 484
	20.8	1	149 150
	44.1	1	28.2 28.0
		506	45.3 44.6
		1025	63.3 69.2
		2008	144 150
		2900	257
	70.3	1	2.65 2.72
19.37	44.1	1	120 121
29.61	44.1	1	225 220 225
39.86	44.1	1	383 372

conditions. Consequently, we have interpolated graphically Gold's rate constants at constant temperature to 44.1% w/w acetone by plotting log k_0 vs. concentration of acetone. The interpolated values are compared with ours on an Arrhenius plot in Fig. 1. The agreement is satisfactory, though Gold's values are somewhat lower than ours.

The Arrhenius energy E_A of the equation

$$\ln k_0 = A\, e^{-E_A/RT},$$

where A is a constant, R is the gas constant, and T is the temperature, decreases with increasing temperature, as found by Gold (9). Our values of E_A calculated from rate constants at adjacent temperatures are given in Table I; they agree well with those of Gold for other acetone concentrations. The entropy of activation $\Delta S^{\ddagger}$ calculated from the equation

$$A = (ekT/h)\, e^{\Delta S^{\ddagger}/R}$$

where k is Boltzmann's constant and h is Planck's constant, is also given; it also decreases as the temperature increases.

The rate constants at constant pressure are plotted on a van't Hoff plot in Fig. 2. The volume of activation at 0° C and 1 b was obtained from the graphically measured slope of the curve at 1 b. It is

$$\Delta V^{\ddagger} = -22.0 \pm \sim 1.5 \text{ cm}^3 \text{ mole}^{-1} \text{ at } 0° \text{ C, 1 b.}$$

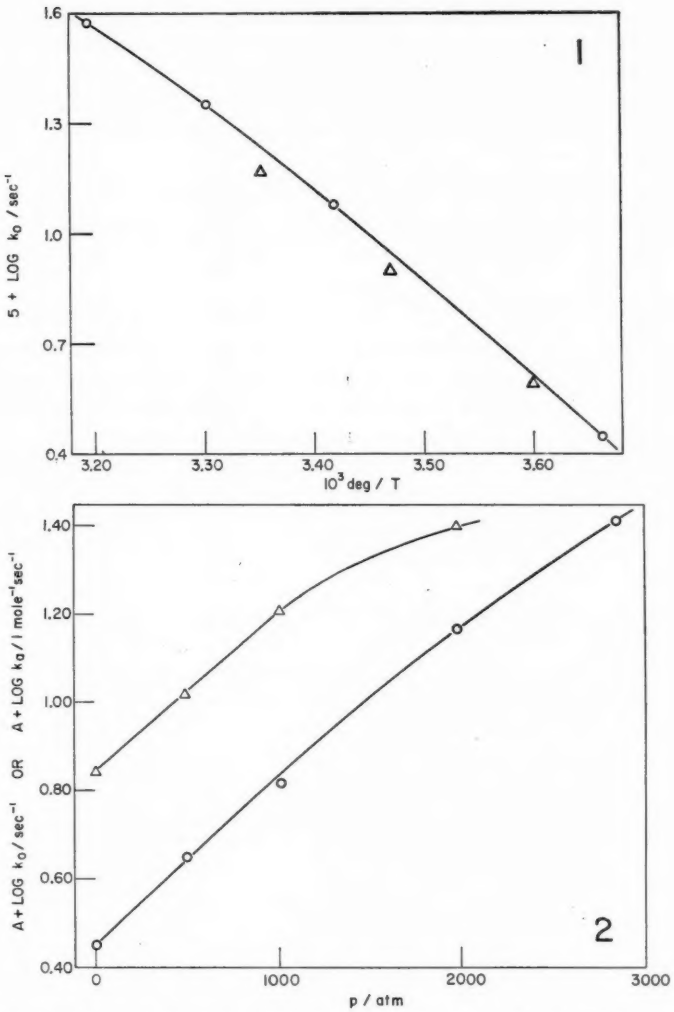


FIG. 1. Plot of log k_0 vs. $1/T$. Crosses: this paper. Circles: interpolated to 44.1% w/w acetone in water from Gold's results.

FIG. 2. Plot of log k_0 and log k_a vs. p. Circles: k_0. Triangles: k_a.

Acid-catalyzed Hydrolysis

The rate constants for the acid-catalyzed hydrolysis are given as a function of temperature, pressure, and solvent composition, in Table II. The acid concentrations are those at the temperature of the experiment and the pressure of 1 atm calculated from concentrations at room temperature using the data of Thomas and McAllister (10) on the volumes of acetone–water mixtures at various temperatures; because the compression of acetone–water mixtures is not known it is not possible to give rate constants under pressure, but only values of $k/c_{H^+}{}^0 = k_a\rho_p/\rho_{1\,b}$, where ρ_p and $\rho_{1\,b}$ are the densities of the solution at the temperature of the experiment and at pressures p and 1 b respectively.

TABLE II

Rate constants for the acid-catalyzed hydrolysis of acetic anhydride

Temp., ° C	% w/w of acetone	p/b	c_{HClO_4}/mole l.$^{-1}$*	$(10^3k/c_{H^+}{}^0)$/l. mole^{-1} sec^{-1}
0	20.8	1	0.1197	0.472
			0.2436	0.498
	44.1	1	0.0980	0.229
			0.1959	0.224
			0.4834	0.228
			0.1718	0.219
			0.2457	0.203
			0.2851	0.229
		506	0.2031	0.328
			0.1011	0.334
		1025	0.1011	0.533
			0.1011	0.525
			0.2390	0.481
			0.2400	0.520
			0.2572	0.506
		2008	0.1011	0.808
			0.2585	0.753
	70.3	1	0.1109	0.0717
				0.0733
19.37		1	0.0954	1.37
			0.0954	1.56
			0.1908	1.39
29.61		1	0.1187	3.70
			0.2319	3.68
39.86		1	0.0945	8.90
			0.1890	9.03

*c_{HClO_4} is that at the temperature of the experiment and 1 atm.

TABLE III

Arrhenius energies and entropies of activation for the spontaneous and acid-catalyzed hydrolyses of acetic anhydride

Temp. range, ° C	Spontaneous hydrolysis		Acid-catalyzed hydrolysis	
	E_A / kcal mole^{-1}	ΔS^* / cal deg^{-1} mole^{-1}	E_A / kcal mole^{-1}	ΔS^* / cal deg^{-1} mole^{-1}
0–19.37	11.95	−37.6	15.34	−21.1
19.37–29.61	10.56	−42.3	16.19	−18.2
29.61–39.86	9.68	−45.2	16.31	−17.8

The Arrhenius energy and the entropy of activation both increase with temperature as shown by the data in Table III, in which E_A and ΔS^* [$= R \ln (A/\text{l. mole}^{-1})(h/ekT)$] calculated from adjacent temperatures are given. The changes are less marked than those for the spontaneous hydrolysis, but seem reasonably certain.

The values of log $k/c_{H^+}{}^0$ as a function of pressure at 0° C are shown in a van't Hoff plot in Fig. 2. The slope of the curve at 0° C and 1 b as measured graphically is

$$RTd \ln (k/c_{H^+}{}^0)/dp = -\Delta V^{\ddagger} + \chi RT = +18.5 \pm \sim 1 \text{ cm}^3 \text{ mole}^{-1}$$

where χ is the compressibility of the pure solvent.

The compression of acetone–water mixtures has been measured only at 1000 atm and 25° C (11) and 30° C (12). The compressibility of acetone has not been measured at

0° C, but it appears from the compilation of McGowan (13) that it will be close to 120×10^{-6} atm^{-1} at 0° C and 1 atm. Newitt and Weale (11) point out that the compression of acetone–water mixtures at 25° C and 1000 atm is roughly linear in the mole fraction. Using this assumption and the compressibility of water at 0° C given by McGowan we find $\chi RT = 1.4$ cm^3 mole^{-1} at 0° C and 1 b. Consequently, for the acid-catalyzed hydrolysis

$$\Delta V^{\ddagger} = -17.1\pm\sim1.3 \text{ cm}^3 \text{ mole}^{-1} \text{ at } 0° \text{ C, 1 b}$$

the uncertainty having been increased to allow for the uncertainty in the compressibility.

4. DISCUSSION

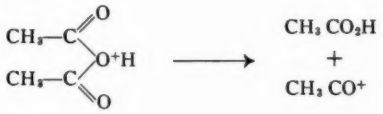
Spontaneous Hydrolysis

The volume of activation, $-22.0\pm\sim1$ cm^3 mole^{-1} at 0° C and 1 b, is very similar to that for the spontaneous hydrolysis of ethylene oxide (14). The mechanism is likely (9) to be the attack of a water molecule on a molecule of acetic anhydride, and a considerable separation of charges occurs. The low volume of activation confirms this; the volume lost due to the formation of a partial valence bond between water and acetic anhydride is expected to contribute only about -5 to -10 cm^3 mole^{-1} to the volume of activation (14), and the remaining part of $\Delta V^{\ddagger}$, -16 to -11 cm^3 mole^{-1}, is presumably due mainly to electrostriction of the solvent.

Acid-catalyzed Hydrolysis

There are many possible mechanisms for the acid-catalyzed hydrolysis of acetic anhydride. The proton can be on either the carbonyl oxygen or the ether oxygen. Either form can react by the A-1 or the A-2 mechanism. The A-2 mechanism can take on several forms according as the incoming water molecule substitutes or adds, and, if it adds, according as the slow step is the formation or decomposition of the adduct.

Gold and Hilton (3) have shown that the rate of hydrolysis in concentrated aqueous acids is nearly proportional to Hammett's acidity function h_0, and is not proportional to c_{H^+}. They assumed that the Zucker–Hammett hypothesis, that rates of A-1 reactions are proportional to h_0 and those of A-2 reactions are proportional to c_{H^+}, holds, and deduced that the slow step is



[4.1]

in which the proton is on the ether oxygen in the reactive conjugate acid. If the slow step were reaction [4.1], then according to arguments developed in Part I of this series (6) and confirmed experimentally for the A-1 hydrolyses of formals, acetals, and ethyl orthoformate in Part II (7), both the volume and entropy of activation would be positive. In fact, both are negative, $\Delta S^{\ddagger}$ being ~-20 cal deg^{-1} mole^{-1} and $\Delta V^{\ddagger}$ being -17.1 cm^3 mole^{-1}. The slow step is not, therefore, reaction [4.1]. The A-1 reaction

[4.2]

is consistent with the experimental ΔV^* and ΔS^* because, due to electrostriction of the solvent, the greatly increased polarity in the transition state would make both the volume and the entropy less than that of the conjugate acid. Thus an A-1 mechanism is possible, but only if a separation of charges occurs in the transition state. The justification of the Zucker–Hammett hypothesis requires that this does not occur, and so it ought not to apply to reaction [4.2]. Consequently, we conclude that the hydrolysis of acetic anhydride is another reaction for which the Zucker–Hammett hypothesis is invalid. We have shown previously that the hydrolyses of ethylene oxide (4) and of diethyl ether (5) do not follow the Zucker–Hammett hypothesis, and Taft, Deno, and Skell (15) refer to other evidence that refutes it. There can be no doubt that the Zucker–Hammett hypothesis does not reliably distinguish between A-1 and A-2 reactions.

The acid-catalyzed hydrolysis of acetic anhydride is formally similar to the acid-catalyzed hydrolysis of aliphatic esters, acetic anhydride being considered as acetyl acetate. It is instructive, therefore, to compare the various quantities of activation of the two hydrolyses. The volume of activation for the hydrolysis of methyl acetate in 44.1% w/w acetone–water is -13.3 cm^3 mole^{-1} at 35° C (16), similar to that for acetic anhydride. The entropy of activation for the hydrolysis of ethyl acetate in 56% w/w acetone–water is, from the data in ref. (17), -26.1 cal deg^{-1} mole^{-1}, again very similar to that for the hydrolysis of acetic anhydride. Unfortunately for a simple explanation of these similarities, the solvent effects are quite different. The logarithm of the ratio of rate constants in 20.8% w/w and 70.3% w/w acetone–water is -0.825 at 0° C for acetic anhydride, while for ethyl acetate it is, from the data in ref. (17), -0.330 at 35° C and for methyl propionate it is, from the data in ref. (18), -0.354 at 25° C. For comparison, the logarithm of the ratio of the *second-order* rate constants for the spontaneous hydrolysis of acetic anhydride is, from our results, -1.284. As we discussed above, the transition state for the spontaneous hydrolysis is probably very polar. The simple conclusion from the volumes and entropies of activation is that the transition state for the hydrolysis of acetic anhydride is similar to that for the hydrolysis of aliphatic esters; the simple conclusion from the solvent effects is that the transition state for the hydrolysis of acetic anhydride is considerably more polar. The resolution of these apparently contradictory conclusions will await more experimental data.

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THE LUMINESCENCE OF COMPLEX MOLECULES IN RELATION TO THE INTERNAL CONVERSION OF EXCITATION ENERGY. PART I[1]

ROBIN M. HOCHSTRASSER

ABSTRACT

The relative fluorescence yields of a variety of double molecules have been measured as a function of the wavelength of exciting light. In some cases the yield from the second excited state is lower than from the first. This effect is attributed to either photodecomposition or to the enhancement of intramolecular energy transfer processes which can compete with the internal conversion between the excited singlet states. The experiments on bianthrone have suggested a method of elucidating the mechanism of the photochromic isomerization of this compound.

INTRODUCTION

The fluorescence of the vast majority of aromatic compounds arises from the radiative transition – first excited singlet to ground (singlet) state. On excitation to higher electronic states this same luminescence is observed and usually with unchanged yield. This implies that the rate of internal conversion to the radiating level is fast compared to the rate of intersystem crossing between upper excited states of different multiplicity. It has been suggested (3) that the fall-off in fluorescence yield of dibromoanthracene excited with light below 3000 Å is due to heavy atom-induced intersystem crossing to the second triplet level. This indicates comparable rates for these competing processes. Preliminary studies have indicated that a variety of molecules which are apparently quite stable photochemically have luminescence efficiencies which are anomolous in terms of the above rule.

In this work the relative luminescence yields of a series of double molecules have been measured as a function of the exciting wavelength. A double molecule is one consisting of two identical parts coupled through a conjugating linkage.

EXPERIMENTAL

The fluorescence measurements were made by illuminating the samples contained in a Vycor tube or silica cell with the beam from a hydrogen lamp and Beckman D.U. monochromater. The luminescence was detected over a 20° region centering at 70° to the main beam by means of an end-on-type photomultiplier with S11 response. The incident radiation was filtered out by 1.5 cm of a saturated solution of sodium nitrite in water. By using suitable Corning filters, the cutoff could be extended to longer wavelengths. This combination provided good cutoff at 3950 Å. The relative quantal output of the hydrogen lamp was known at each wavelength from 2500–3800 Å in terms of the luminescence of pure anthracene, which is known to be constant over this region (3, 4). The range was extended to 4100 Å by calibrating the lamp output against the luminescence intensity from a totally (99%) absorbing solution of tetracene. The fluorescence yield of tetracene is independent of the exciting light wavelength in this region of its absorption. The hydrogen lamp becomes less continuous above 3700 Å but good reproducibility could be obtained by opening up the monochromater slit for this range of excitation. All the solutions which were studied absorbed at least 99% of the incident light throughout the exposed pathlength. The solvents were ethyl alcohol or petroleum ether. The low temperature experiments were performed in a quartz Dewar with an optically clear

[1]*Manuscript received March 16, 1959.*
Contribution from the Department of Chemistry, University of British Columbia, Vancouver, B.C.

base. Rigid glasses were either alcohol, ether–alcohol, or E.P.A., depending on solubility of the compound. The same results were obtained from cracked and optically clear rigid glasses. Luminescence measurements may be radically affected by small amounts of impurities. The criterion for purity in this work was taken to be reproducibility after two further purifications by different methods. These methods involved recrystallization, sublimation, and chromotography. III, VI, VII, VIII, IX, and X were synthesized by Dr. Y. Matsunaga. IV and V were synthesized according to the method of A. Willemart (12). They were purified on alumina. I and II were Delta chemicals samples with fluorescent impurities. The fluorescence spectrum of each substance was examined on a Cary Recording Spectrometer. In no case did the spectrum of the purified material change when the wavelength of the exciting light was altered.

RESULTS AND DISCUSSION

Plots of the relative luminescence yields against exciting wavelength are shown on Figs. 1–3. Some of the curves show slight variations of the order of 3% which cannot be taken as real under the present experimental conditions.

(*A*) *1,1-Binaphthyl* (I); *2,2-Binaphthyl* (II); *α,α-Di-β-naphthol* (III)

These substances have long absorption tails and there is an unusually large separation of absorption and fluorescence, indicating substantial distortion in the excited state. The fluorescence yields of (I), (II), and (III) crystals at 25° C and −183° C were independent of exciting light. Alcoholic solutions and rigid glasses of (I) and (III) also retained constant yields of emission over the range 2500 Å–3500 Å.

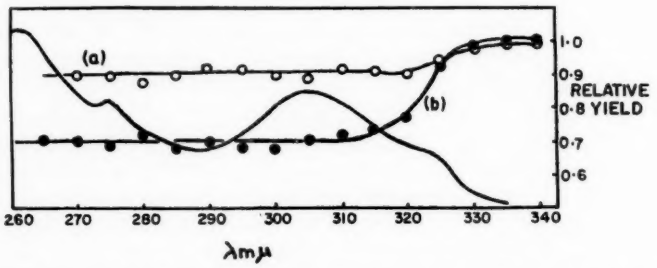


FIG. 1. The variation of the fluorescence yield of 2,2-binaphthyl with wavelength of exciting light. (*a*) crystal (*b*) alcohol solution or rigid alcohol glass. Smooth curve is the approximate absorption spectrum of 2,2-binaphthyl with log (extinction) as abscissa.

The results for (II) are given in Fig. 1. The fluorescence yield is constant to about 3275 Å, and below this exciting wavelength the luminescence falls off by about 30%. This is the type of effect that would be observed if an impurity was emitting above 3200 Å. Commercial (II) is green and even after many recrystallizations the color is greenish, although no impurities can be detected by absorption in a 10-cm path. After purification on alumina, one can obtain with difficulty colorless crystals with a bluish tinge. Such phenomena are reminiscent of the effects of very small quantities of tetracene in anthracene where energy transfer is highly efficient (1). The appearance of the blue fluorescence was accepted as a criterion of purity in this case. The absorption spectrum of (II) differs from (I) in the same manner as that of biphenyl differs from benzene. Free rotation of one ring relative to the other is sterically allowed and conjugative

interaction may occur, resulting in a red shift of the spectrum (5). It is feasible that the double molecule (II) has two closely lying electronic states at low energies. Such a splitting could arise through a weak interaction between the ring systems and if this is the case electric dipole transitions to one of these states may be more or less forbidden than transitions to the other state, depending on the degree of interaction (7, 9). The results indicate that there is an enhancement of the fluorescence when the excitation is in the long wavelength tail, that is, in the region of the 0–0 transition. It is possible that population of the upper state vibrational levels which are always below the crossing line of the singlet and triplet energy surfaces can occur in this case. In any case this system deserves detailed individual study and will be discussed in a future part of this series.

(*B*) *9,10-Di-α-naphthylanthracene* (IV); *9,10-Di-β-naphthylanthracene* (V); *9,9′-Dianthryl* (VI); *9,9′-Dianthran-10,10-diol* (VII)

The quantum yields of these compounds are independent of the wavelength of exciting light from 2600 to 3900 Å. This conclusion applies to crystals at 25° C and −183° C, alcoholic solutions at 25° C, and to rigid alcohol glasses. The actual quantum yields of luminescence from all but VII were higher than that of anthracene.

(*C*) *trans-Stilbene* (VIII); *p-Dimethoxystilbene* (IX); *Di-α-ethoxynaphthostilbene* (X); *α,β-Bis (9,9′-anthronylidene)-ethane* (XI)

No fluorescence could be detected from XI crystals below 6000 Å.

The luminescence yields in Fig. 2 relate to alcoholic solutions of X and XI and crystals of IX at −183°. There is little difference between rigid glass and viscous solution except in relation to the absolute fluorescence yield which is always greater in the glass. It

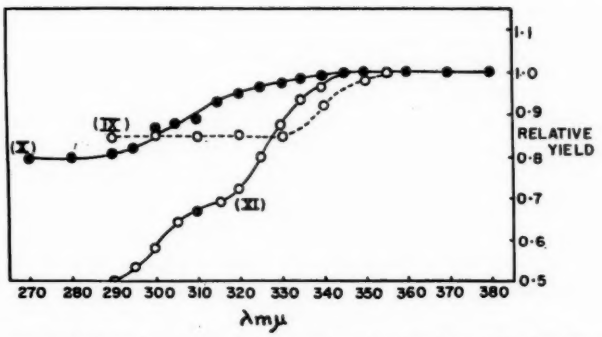
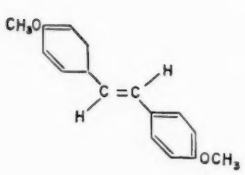


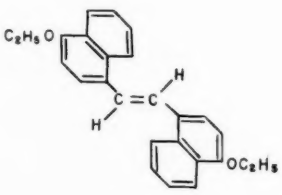
FIG. 2. Fluorescence yields as functions of the wavelength of exciting light for IX, X, and XI.

can be seen that double molecules of this type exhibit a marked wavelength dependence, which may be due either to photochemical reaction in upper excited states or to an intramolecular energy transfer process which is much more efficient in the upper excited state than in the fluorescent state. With the exception of XI, which is in any case too complex a molecule to permit a detailed study, it is felt that the fall-off in fluorescence yield may be caused by a lowering of the potential energy barrier to rotation about the ethylenic double bond in the upper excited states. The different results obtained with VIII on the one hand and with IX and X on the other would be attributed to the double bond character of the ethylenic link in each of these types. The naphthalenic groups will certainly be out of plane even in the trans form and consequently there will be less

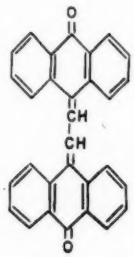
conjugative interaction through the central double bond. If the time spent in an upper excited state is of the order of 10^{-12} seconds then the frequency of twist must be of the same order as a few hundred vibration frequencies if the fall-off in yield is due to this process. This corresponds to a considerable lowering of the barrier. The phosphorescence contribution to the total luminescence curve in Fig. 2 must be negligible under these experimental conditions as the same curve was obtained in solution at room temperature and in rigid glasses at liquid nitrogen temperature. In all cases no permanent changes in the absorption spectrum could be detected which would have indicated a photoprocess occurring with a significant quantum yield. Some experiments were done using completely oxygen-free solutions and no differences were obvious. In the case of *trans*-stilbene the fluorescence yield was constant throughout the absorbing region. The fluorescence yield was also measured as a function of temperature for crystalline VIII and no discontinuities were observed.



IX



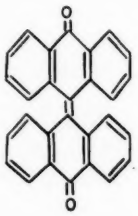
X



XI

(*D*) *Bianthrone* (XII)

This substance is photochromic (6), thermochromic (11), and photochemically reactive (12). The bianthrone used in this work was recrystallized twice from dichloroethane, sublimed *in vacuo*, then chromatographed twice on alumina. Even under these conditions a fluorescent impurity was shown to be present. (XII) did not fluoresce in solution at 25°, i.e. the apparatus would detect very low light levels corresponding to fluorescence yields of the order of 10^{-3}. In ether–isopentane glass at −183° C the fluorescence yield varied with exciting energy in the manner shown in Fig. 3 along with the absorption spectrum of bianthrone.



XII

The fluorescence yield is constant throughout the first absorption band but falls off to about 50% of this value below 3400 Å. During irradiation in the low energy band the so-called colored form of bianthrone is being produced, and the constancy of the luminescence yield indicates that the process of photochromism is also independent of

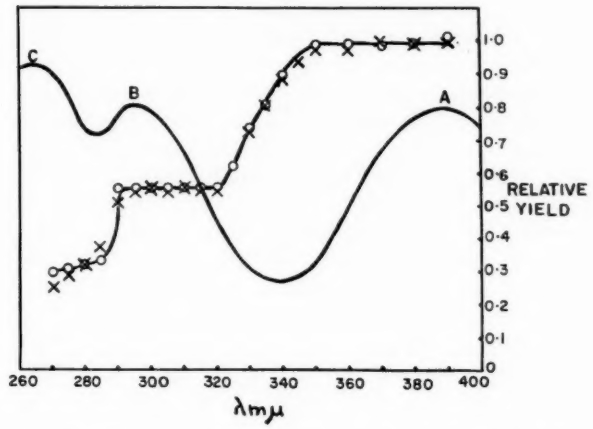


FIG. 3. The fluorescence of bianthrone as a function of the wavelength of exciting light.
○ In ether–isopentane glass.
× After U.V. irradiation in non-rigid medium.
— Absorption spectrum of bianthrone. The absorption at A corresponds to a $n \rightarrow \pi^*$ transition while B and C are probably $\pi \rightarrow \pi^*$.

the excitation energy over this region; such considerations will apply if only the formation of the photochromic isomer is in competition with fluorescence. The similarity of the fluorescence curves for bianthrone in ether–isopentane and the pre-irradiated sample—which is green due to reversion to photochromic isomer—indicates that the same fluorescence is being observed in each case. The actual yield was diminished slightly owing to reabsorption by the long wavelength band of the colored form. The absorption band at 2950 Å is due to a higher electronic transition, and either an internal conversion process, *other* than the rearrangement of the electronic excitation of this state into the vibrational modes of the fluorescent state, is occurring *or* the probability of photodecomposition is enhanced by exciting the molecule to this state. Here again the barrier to isomerism may be very slight in the higher levels of excitation. This is tantamount to an increased probability of intersystem crossing in the upper state as it is likely that the photochromic isomer is the molecule in its lowest triplet state. Hirshberg and Fischer (6) point out that no photochemical reactions other than photochromism occur at low temperatures.

CONCLUSIONS

As a rule the fluorescence yield is independent of the wavelength of the exciting light. Some double molecules have provided striking exceptions to this rule. The exceptions have arisen in the first place when there is slight conjugative interaction between two aromatic ring systems; e.g., 1,1′-binaphthyl exhibits normal behavior while 2,2′-binaphthyl is exceptional. Secondly, exceptions also arise when the molecule can be photochemically isomerized, e.g., naphthostilbene and bianthrone respectively.

It is likely that the configurations of the latter type of molecule in the excited states will differ markedly from those in the ground state. In particular the relative orientation of the ring systems may change considerably. This consideration is supported by the large separation of emission and absorption for the compounds studied here.

That some of the phenomena reported here may be due in part to an enhancement of the rate of intercombination between states of different multiplicity may only be considered as an interesting conjecture at this stage. It is likely that deformation of a π-molecular orbital, such as in the case of the trinitrobenzene complexes of aromatic hydrocarbons (10), could result in a considerable increase in the rate of intersystem crossing. With molecules such as naphthostilbene and bianthrone this rate may be unusually great in the upper excited states if there is a reasonable distortion. Such a distortion would necessarily increase the π–σ interactions in the molecule and it is known that the main contribution to the spin orbital coupling in these molecules arises from interactions of this type (8).

It has been the purpose of the first part of this paper to present the results of fluorescence studies on a variety of double molecules. It is apparent that a detailed study of the photochemistry of some of these systems will be necessary before more certain conclusions can be reached. Subsequent parts of this series will describe such studies as well as results on the phosphorescence of these and similar molecules and new results on the phosphorescence and fluorescence of N-heteroaromatics and their derivatives.

ACKNOWLEDGMENTS

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NOTES

THE LOW TEMPERATURE PREPARATION OF ANHYDROUS TITANIUM IV BROMIDE AND ANHYDROUS TITANIUM IV IODIDE FROM BENZENE SOLUTIONS

KARL H. GAYER AND GERALD TENNENHOUSE

A recent series of experiments required supplies of anhydrous titanium IV bromide and anhydrous titanium IV iodide. The usual methods for preparing titanium IV bromide by passing either bromine vapor or hydrogen bromide gas over a heated mixture of titanium dioxide and carbon or titanium metal were found to be too time-consuming for frequent use. Consequently the following method was devised.

EXPERIMENTAL

Preparation of Titanium Tetrabromide

The following experimental procedures, which required an inert atmosphere, were carried out in a dry box in which the air had been dried over P_2O_5. Hydrogen bromide gas, flowing at approximately 350 cubic centimeters per minute, was dried by being passed through a porous tower of phosphorus pentoxide. This dry gas was directed into the reaction vessel.

A solution of titanium IV chloride was made by adding 35 g of redistilled titanium IV chloride to 71 g of reagent grade benzene in a 250-ml two-necked flask. The flask was maintained at 0° C by means of a salt–ice bath. Hydrogen bromide gas was bubbled into this solution. After 20 minutes of gassing the solution had turned from colorless to yellow to red. After 1 hour, the gassing was stopped and the solution permitted to rise in temperature to 25° over a period of 3 hours. The benzene was distilled off. This was followed by the titanium IV bromide. The portion boiling between 229° and 232° was collected. The product obtained in 80% yield based on $TiCl_4$ was found to melt at 39° C and boil at 231° C. The literature (1, 2) lists the melting point and boiling point as 39° C and 230° C respectively. The compound was analyzed gravimetrically for both titanium and bromide. The following are mean values of three determinations:

Calculated values for	Ti = 13.03%	Br = 86.97%
Experimental values for	Ti = 13.17%	Br = 86.81%

The anhydrous product is an orange-red solid at room temperature, which sublimes readily and is extremely hygroscopic, fuming strongly in air. It is soluble in acetone and ether. It could not, however, be crystallized from these solvents. Furthermore, the product is soluble without reaction in benzene and carbon tetrachloride.

Preparation of Anhydrous Hydrogen Iodide

Anhydrous hydrogen iodide free of elementary iodine was prepared by distilling a mixture of 80 g of reagent potassium iodide in 400 ml 85% phosphoric acid. The resulting product, slightly contaminated with water and iodine, was purified by passing it over an intimate mixture of red phosphorus and iodine, then through a condenser maintained at 0° C to remove iodine, and finally over phosphorus pentoxide.

Preparation of Titanium Tetraiodide

The hydrogen iodide prepared above was bubbled (at approximately 400 cc per minute) into a round-bottom flask containing 35 g of redistilled titanium IV chloride and 88 g

of reagent grade benzene. The flask was kept at 0° C by means of an ice–salt bath. After 5 minutes, the solution had turned dark. The addition of hydrogen iodide was continued for 1 hour. After the mixture had been left to stand for 30 minutes at 0° C, it was freed of excess hydrogen iodide by vigorous gassing with dry nitrogen. The mixture was kept overnight at 0° C after which the titanium iodide was filtered off. The product was recrystallized, then dried under reduced pressure of 25 mm Hg, and sealed in a bent glass tube about 30 cm in length. Finally, the product was sublimed by immersing one end of the tube in an ice–salt bath while gently heating the other end. The purple solid collected in the cold part of the tube. A 70% yield, based on $TiCl_4$ was obtained. Analysis: The titanium was precipitated as the oxide, ignited, and weighed. The iodide was determined by preliminary oxidation with KIO_3, followed by titration with standard $Na_2S_2O_3$ solution. The following are mean values of three determinations:

Calculated values for	Ti = 8.62%	I = 91.38%
Experimental values for	Ti = 8.49%	I = 91.46%

The product is extremely hygroscopic, fuming strongly in air. It is readily soluble in water, forming a brown-colored solution. On standing for several weeks out of contact with the air, the brown solution becomes colorless. The product is soluble without reaction in benzene and carbon tetrachloride.

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A NEW SYNTHESIS OF 5-HYDROXYTRYPTOPHAN*

GERASSIMOS FRANGATOS AND FRANCIS L. CHUBB

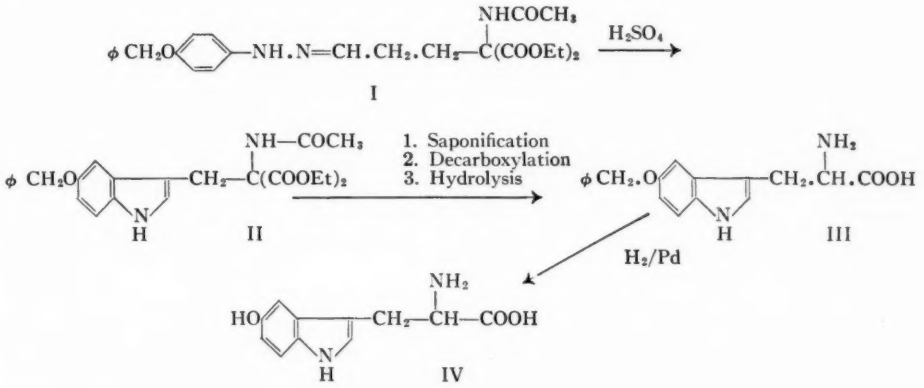
The biological significance of 5-hydroxytryptophan has been established. It is an important metabolite of tryptophan and is a precursor of serotonin (5-hydroxytryptamine) (1). In recent years serotonin has been the subject of an extensive study by many workers due to its potential importance in the function of the autonomic and central nervous system (2).

The first synthesis of 5-hydroxytryptophan was reported by Ek and Witkop (3), and is an application of the gramine synthesis developed by Snyder and Smith (4). A second synthesis of 5-hydroxytryptophan, which is also an application of the gramine synthesis, has recently been reported by Koo, Avakian, and Martin (5). The synthesis herein reported is an application of the convenient tryptophan synthesis of Warner and Moe (6). This method eliminates the difficult and tedious preparation of 5-benzyloxyindole.

The *p*-benzyloxyphenylhydrazone of γ,γ-dicarbethoxy-γ-acetamido-butyraldehyde (I) was prepared, and cyclized, without isolation, to form ethyl β-(5-benzyloxyindolyl-3)-α-carbethoxy-α-acetamidopropionate (II). This was identical with material prepared

**Based on a paper presented at the 41st Annual Conference of the Chemical Institute of Canada, Toronto, May 26–28, 1958.*

from the reaction of ethyl acetamidomalonate with 5-benzyloxygramine. Saponification and partial decarboxylation of II, followed by hydrolysis of the acetamido group, gave 5-benzyloxytryptophan (III). 5-Hydroxytryptophan (IV) was obtained by hydrogenolysis of III.



EXPERIMENTAL

Ethyl β-(5-Benzyloxyindolyl-3)-α-carbethoxy-α-acetamidopropionate (II)

A mixture of 85 g of ethyl acetamidomalonate (4), 0.4 g of sodium methoxide, and 200 ml of absolute ethanol was cooled to 0° with stirring. A thin slurry formed and then 31 ml of acrolein was added during 1.5 hours, keeping the temperature at 0–3°. The stirring was continued for 2 hours at 0–3°. Then 85 g of *p*-benzyloxyphenylhydrazine (7) and 10 ml of glacial acetic acid were added with vigorous stirring. The reaction mixture was heated to 50°, with stirring, and maintained at that temperature until the hydrazine went into solution. The resulting dark solution of II was kept at room temperature overnight. It was then transferred to a three-necked flask and water was added to bring the total volume to 1.5 liters. After 70 ml of concentrated sulphuric acid was added, the mixture was stirred vigorously and refluxed for 3 hours. The ethyl β-(5-benzyloxyindolyl-3)-α-carbethoxy-α-acetamidopropionate soon crystallized. The reaction mixture was cooled and filtered to yield 160 g of crude product. Three recrystallizations from toluene followed by one from aqueous ethanol gave 135 g (75.5%) of pure II, m.p. 169°, undepressed on admixture with an authentic sample prepared according to ref. 5. Anal. Calculated for $C_{25}H_{28}N_2O_6$: C, 66.36; H, 6.24; N, 6.19. Found: C, 66.60; H, 6.28; N, 6.08.

5-Benzyloxytryptophan (III)

The ester II (50 g) was saponified, decarboxylated, and deacetylated according to the procedure of Koo, Avakian, and Martin (5). The intermediate dicarboxylic acid was not purified before decarboxylation and deacetylation to form 5-benzyloxytryptophan (III).

The crude III was purified according to the following procedure. 5-Benzyloxytryptophan (20 g) was warmed with 100 ml of water and 1 liter of ethanol. If solution was not complete then 1% sodium hydroxide was added dropwise until the material all dissolved. After treatment with charcoal and filtration, the solution was cooled and adjusted to pH 6.6 with acetic acid. The 5-benzyloxytryptophan began to crystallize

immediately. In case it separated as a gel, warming and stirring converted it to the crystalline form. A total of 29 g (88.5%) of III, m.p. 276–280° was obtained.

5-Hydroxytryptophan (IV)

5-Hydroxytryptophan was prepared by catalytic hydrogenolysis of III according to the procedure of Koo, Avakian, and Martin (5).

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THE EFFECT OF AMINES AND PHENOLS ON THE GAS-PHASE OXIDATION OF *n*-BUTANE AND ISOBUTANE*

K. U. INGOLD AND I. E. PUDDINGTON

In recent years the antiknock efficiency of a large number of fuel additives has been measured. Among the more powerful fuel additives are amines both aliphatic and aromatic (1, 2, 3, 4), and aromatic compounds in general (2, 5).

From an examination of the high and low temperature oxidation of diisopropyl ether, Chamberlain and Walsh (6, 7) concluded that inhibition of this reaction by aromatic compounds and, therefore, the antiknock ability of aromatic compounds, was due primarily to the electronic properties of the ring, nitrogen, and other side groups merely modifying the properties of the ring. However, it has since been shown by using deuterated amine antiknocks that, in the internal combustion engine, aromatic amines owe their antiknock efficiency to their ability to destroy chain-propagating radicals ($X^{\cdot}$) by the reaction (3)

$$X^{\cdot} + ArNHR \rightarrow XH + Ar\dot{N}R \qquad [1]$$

where $Ar\dot{N}R$ is a less reactive radical than $X^{\cdot}$. The effect of deuterated antiknocks on the low temperature oxidation of hydrocarbons has, however, not been previously studied.

The present work involved a brief investigation of the effect of aniline and aniline N—D_2 on the low temperature oxidation of two simple paraffins, viz. *n*-butane and isobutane. The effect of a few other amines and phenols was also examined with a view to comparing inhibitor efficiencies in gas- and liquid-phase (8) hydrocarbon oxidations.

The oxidation was studied in a conventional apparatus, except that the progress of the reaction was measured by means of a diaphragm manometer to avoid contamination of the reaction vessel with mercury. The butane (70 mm) and oxygen (280 mm) were premixed before being admitted to the cylindrical Pyrex reaction vessel (15 cm long, 4 cm diameter). The oxidation of *n*-butane was studied at 275° C and isobutane in the range 275°–310° C. The pressure–time curves for both butanes are S-shaped, and although the

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rate of pressure increase is at first very small, there is no initial decrease in pressure at these temperatures. The onset of a pressure increase has been shown (9) to mark a transition from a surface-inhibited reaction to an autocatalytic reaction in which effects resulting from chain-branching predominate and surface effects are much less important. For this reason, the amines and phenols were added not only at the start of the reaction ($\Delta p = 0$) where their effect might be due to their action on the surface, but were also added during the course of the reaction after a definite pressure increase had occurred and the induction period was over.

Since most of the additives had rather low vapor pressures at room temperature, they were stored in traps separated from the reaction vessel by metal valves; both traps and valves could be heated to 100° C. Helium at 1 atmosphere pressure was admitted to the traps and after residence for at least half an hour was used to carry the additive into the reaction vessel. Induction periods (defined as the time required for a pressure increase of 1.0 mm) are summarized in the table, all values being averages of at least two experiments.

TABLE

Effect of amines and phenols on the induction period of *n*-butane and isobutane
(Butane 70 mm, oxygen 280 mm, helium 180 mm)

Additive	Additive pressure (mm)	Added at Δp (mm)	*n*-Butane (275° C) induction period (seconds)	Isobutane (310° C) induction period (seconds)
None	—	—	140	400
He	—	0	125	140
He + aniline	9.0	0	1620	3900
He + aniline N—D_2	9.0	0	1090	2350
He + phenol	9.0	0	210	270
He + *o*-toluidine	4.5	0	750	1100
He + N-methylaniline	4.5	0	700	1200
He + *p*-cresol	3.5	0	160	185
He + piperidine	9.0	0	440	30
He + pyrrole	9.0	0	650	150
He + ammonia	9.0	0	165	110
He	—	2.7	20	10
He + aniline	9.0	2.7	110	250
He + aniline N—D_2	9.0	2.7	100	200
He	—	4.5	16	5
He + aniline	9.0	4.5	64	160
He + phenol	9.0	4.5	36	9
He + *o*-toluidine	4.5	4.5	55	40
He + N-methylaniline	4.5	4.5	60	40
He + *p*-cresol	3.5	4.5	22	7
He + piperidine	9.0	4.5	90	5
He + pyrrole	9.0	4.5	84	15
He + ammonia	9.0	4.5	30	5

Analysis of the reactants at the end of the induction period showed that the addition of aniline at the start of the reaction decreases the rate of butane consumption during the induction period. Aniline is, therefore, a true inhibitor for the oxidation of both butanes.

The reduced inhibiting effect of aniline N—D_2 compared with aniline shows that the rate-controlling step of at least a part of the inhibition must involve rupture of the N—D or N—H bond. This result is in agreement with the results of Brown *et al.* (3) on the antiknock efficiency of N-methylaniline and N-deutero-methylaniline. Although the conclusions of Walsh (7) that aromatic compounds inhibit by virtue of the electronic properties of the ring are not invalidated, this factor would seem to be of little importance with aromatic amines.

Since the isotope effect exists when aniline is added, both at the start of the reaction and during its course when surface effects are at a minimum, inhibition probably occurs to a fairly large extent in the gas phase. The reduction in the isotope effect when aniline is added during the reaction suggests that some exchange may occur, probably on the walls between the deuterated aniline and the various oxygenated products. The isotope effect is somewhat less than when aniline is used to inhibit liquid phase oxidations (8).

The results obtained with aniline, phenol, N-methylaniline, and *p*-cresol, all of which have also been studied in the liquid phase (8), show that the range of inhibitor efficiencies is smaller in the gas than in the liquid phase. By analogy with the results obtained with aniline these additives also probably inhibit by way of reaction [1].

Pyrrole and piperidine were studied to see if there was any correlation between the base strength of amines and their inhibiting efficiency. These two compounds have similar inhibiting power on the oxidation of diethyl ether (10) yet pyrrole is an extremely weak base while piperidine is a strong base. Both amines inhibit the *n*-butane oxidation. At 310° C pyrrole has only a small inhibiting effect on isobutane, while piperidine behaves as a strong catalyst. The catalytic action of piperidine occurs at temperatures as low as 275° C where, judging by the results with *n*-butane, the piperidine itself is probably not decomposed or oxidized appreciably. At low temperatures pyrrole also becomes a catalyst, although a rather weak one. For example, at 297° C the induction period for isobutane with helium alone is 1400 seconds, for pyrrole 1000 seconds, and for piperidine 100 seconds. The catalysis by both amines is not likely to be due to their decomposition, since such catalysis would be expected to increase with temperature. Ammonia, also, acts as an inhibitor with *n*-butane and as a catalyst with isobutane. The difference in behavior of these three compounds with the two butanes suggests that different intermediates are involved in the oxidation of the butanes. Inhibition of the *n*-butane oxidation may be due to reaction [1]. The catalysis observed with isobutane suggests that a catalyzed decomposition of the chain-branching intermediate is of considerable importance.

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